THE MEDICAL JOURNAL OF AUSTRALIA

VOL. I.—47TH YEAR SYDNEY, SATURDAY, APRIL 16, 1960 No. 16

Table of Contents

[The Whole of the Literary Matter in THE MEDICAL JOURNAL OF AUSTRALIA is Copyright.]

ORIGINAL ARTICLES— Page

Patent Ductus Arteriosus, by Douglas Cohen 601
Modern Concepts of Placenta Prævia, by L. Woodrow Cox 605
Demonstration of the So-Called Bile Canaliculi, by E. B. Jones 611

REPORTS OF CASES—

Ataxia-Telangiectasia, by John Beveridge 613
Hamman-Rich Syndrome (Diffuse Interstitial Pulmonary Fibrosis), by W. M. Maxwell and P. E. Campbell 616
A Case of Rhesus Incompatibility Occurring in a Twin Pregnancy, by R. S. Hyslop and W. Whiley 622

REVIEWS—

Peripheral Vascular Diseases 624
Leprosy in Theory and Practice 624

BOOKS RECEIVED 624

LEADING ARTICLES—

The Waiting People 625

CURRENT COMMENT—

Prednisolone and Aspirin in Rheumatoid Arthritis 626
Scurvy and Its Prevention 626
Darwin's Illness 627

ABSTRACTS FROM MEDICAL LITERATURE—

Pædiatrics 628
Physiology 629
Biochemistry 629

PUBLIC HEALTH—

Some Aspects of Epidemiology and Preventive Medicine Abroad 630

BRITISH MEDICAL ASSOCIATION— Page

Victorian Branch 633

OUT OF THE PAST 634

SPECIAL CORRESPONDENCE—

Paris Letter 634

CORRESPONDENCE—

"Tofranil" 636
General Pharmaceutical Benefits 636
The Problem of Injury and Accident 637
The Meeting of the Federal Council 637
Medical Research in Australia 638

MEDICAL MATTERS IN PARLIAMENT—

House of Representatives 638

POST-GRADUATE WORK—

The Melbourne Medical Post-Graduate Committee 638
The Post-Graduate Committee in Medicine in the University of Sydney 639

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA 639

NOTES AND NEWS 640

MEDICAL PRACTICE—

Police Offences (Amendment) Act, 1908, of N.S.W. as Amended 640

NOMINATIONS AND ELECTIONS 640

DIARY FOR THE MONTH 640

MEDICAL APPOINTMENTS: IMPORTANT NOTICE .. 640

EDITORIAL NOTICES 640

PATENT DUCTUS ARTERIOSUS.[1]

By DOUGLAS COHEN, M.S., F.R.A.C.S.,

From the Adolph Basser Institute of Cardiology and the Institute of Child Health, Royal Alexandra Hospital for Children, Sydney.

WHEN Robert Gross (1940) tied the first patent ductus arteriosus in 1939, it may fairly be said that the modern era of cardiac surgery had begun. Prior to this time, attempts to correct congenital or acquired abnormalities of the heart had been infrequent and usually disastrous. The diagnosis and treatment of the uncomplicated ductus are now relatively simple and safe; but it is becoming increasingly apparent that a variety of complications may alter both the clinical picture and the method of management.

The Uncomplicated Patent Ductus.

This is one of the few congenital heart lesions that can be diagnosed with certainty on clinical signs alone. The classical machinery murmur described by Gibson so long ago is diagnostic and will be found to be present in almost every case. However, certain exceptions will be referred to later. The peripheral signs are also very characteristic. The increased pulse pressure gives rise to a strong, thrusting radial pulse, and the increased amplitude of the blood pressure is also expressed by the presence of palmar pulsation, as described by Stuckey, the superficial palmar arch being easily palpable; in infants, this is an extremely helpful sign, when accurate estimation of the blood pressure may be difficult. The electrocardiogram and X-ray findings in the chest may be within normal limits if the ductus is small; but there is usually a mild to moderate degree of cardiac enlargement, with some fullness in the region of the pulmonary artery, while any degree of left ventricular preponderance in the electrocardiogram is usually an indication of a substantial left-to-right shunt. Any evidence of right ventricular overactivity in the electrocardiogram is an indication for further investigation. If the case appears to be a straightforward one and no complications are suspected, we do not think it is necessary to go any further to establish a firm diagnosis, and recommend treatment. Cardiac catheterization is undertaken only when the presence of some complication is suspected.

Indications for Operation.

All patients with uncomplicated patent ductus arteriosus should receive the benefits of surgery. Provided that the operation is performed by a surgeon experienced in the techniques of cardio-vascular surgery, the risks of opera-

[1] Based on a paper read at a meeting of the Section of Pædiatrics, Australasian Medical Congress (B.M.A.), Tenth Session, Hobart, March 1 to 7, 1958.

tion are slight, post-operative morbidity is minimal and recurrence is unlikely. The patient is thus given a normal expectancy of life. Many investigators have shown that, after the first year of life, the chances of a patent ductus closing spontaneously are remote, and the various complications associated with this condition will probably result in the death of the patient in early adult life (Campbell, 1955). It has been our experience that the ideal time for operation is between the ages of one and three years, provided that the diagnosis has been made early enough. Indeed, we now recommend surgery as soon as the patent ductus has been positively diagnosed, since there are certain risks in procrastination. We have, on two occasions, seen children die from fulminating staphylococcal pneumonia whilst awaiting surgery for patent ductus, and one cannot help feeling that the presence of the ductus may have been a very real factor in militating against their survival. When operation is undertaken under the age of four years, it can be performed through a vertical axillary incision, which gives a much superior result from the cosmetic point of view and provides an exposure at least as adequate as the standard lateral thoracotomy. Over the age of four years the exposure is, as a rule, not so satisfactory, and the standard approach is preferred. Other points in favour of operation at this early age are: (i) there is less time for complications to develop; (ii) there is no interference with schooling; (iii) parental anxiety is quickly relieved, and the chances of the child's being turned into a "cardiac invalid" are correspondingly reduced. In addition, young children seem to stand thoracotomy much better than older children, and are very little disturbed by the procedure. Also, any limitation of growth and normal development due to the presence of the ductus is quickly overcome when the cause is promptly eradicated (Adams and Forsyth, 1951). When there is any evidence of cardiac failure, however slight, every effort should be made to relieve this prior to operative intervention. A week or more spent in making the patient safe for surgery is well worth while, and considerable judgement is often required in timing surgical intervention in these cases. It will be found, as a rule, that under treatment with digitalis, mercurials and a low sodium intake, steady improvement will take place for a time, after which the patient will start to regress again. The surgeon must be prepared to intervene promptly when it is judged that the maximum degree of improvement has been obtained.

Operative Technique.

The chest is usually entered through the fourth intercostal space or the fourth rib bed (without removal or division of the rib), a vertical axillary incision as described by Denis Browne (1951) being utilized, or a standard lateral thoracotomy, according to the age and habitus of the child. Once the chest has been entered, the upper lobe of the left lung is covered with a moist sponge and held gently out of the operative field with a malleable retractor, great care being taken not to exert any pressure on the heart. The thrill caused by the ductus is next felt for; it is most evident as a rule over the pulmonary trunk and left main branch of the pulmonary artery. The mediastinal pleura is now divided over the descending aorta, behind the vagus nerve, the incision being extended well up along the subclavian artery. The vagus nerve is next clearly displayed. It will be found that there is a distinct layer of fascia beneath the mediastinal pleura, covering aorta and ductus, and it is important deliberately to incise this over the aorta, to enter the correct plane to facilitate dissection of the ductus. This sheet of fascia can be picked up with traction sutures and utilized to draw the vagus nerve and its recurrent branch medially well out of danger. A blunt divulser is then used to clear the ductus, and two number 16 plaited silk ligatures are passed around it. The ductus is now temporarily compressed, to make sure that the action of the heart is unaffected by its obliteration and that the continuous thrill disappears. Once it is certain that ligation of the ductus will produce no adverse effects, the thick silk ligatures are carefully snugged up and tied as tightly as possible, the one at the aortic end being dealt with first. After the ties are in place, it will be seen that the ductus is occluded over a wide area. I am sure it is for this reason, and because the thick ligatures used can be safely tied very tightly without risk of cutting into the ductus, that this method is so effective in obtaining permanent closure of the ductus. The technique described is based on that used by Mr. David Waterston at the Hospital for Sick Children, Great Ormond Street, London, where I understand that there have been no recurrences in more than 200 cases. I have myself used it in over 100 cases, with only one recurrence, as detailed later.

Post-Operative Management.

Drainage of the chest to an under-water seal is provided in all cases. The drainage tube is usually removed in 24 hours, provided that clinical examination and an anteroposterior X-ray film of the chest indicate full lung expansion, and that drainage is not excessive. A broad-spectrum antibiotic cover is provided for several days. The child is returned from the operating theatre on his own bed and placed in an oxygen tent for several hours. There is frequently a transient rise in blood pressure and pulse rate; but these are usually back to normal by the following day. An electrocardiogram is taken as a routine measure a few hours after operation. Usually, after the first 24 hours no special precautions are necessary, and the child is as a rule ready for discharge from hospital when the sutures are removed on the eighth day after operation.

The Infantile Ductus.

Many children present with symptoms of cardiac failure in the first year of life, and a proportion of these will be found to be suffering from patent ductus arteriosus (Powell, 1954). It is important to distinguish this group, since prompt surgery can be life-saving and curative. In this age group the auscultatory findings are rarely typical, and the presence of a fully developed continuous murmur is unusual. In most instances, a long substantial systolic murmur is present, often tending to run over into diastole. Reliance must be placed on the peripheral signs. The presence of palmar pulsation, as described by Stuckey (1957), and of a wide-amplitude peripheral pulse is always very suggestive of the presence of a patent ductus arteriosus. The electrocardiogram will usually show evidence of left ventricular strain unless pulmonary hypertension or some other complication is also present, and the X-ray film will show marked cardiomegaly, with obvious fullness in the region of the pulmonary artery and definite evidence of pulmonary plethora. These children frequently present with feeding difficulties or failure to thrive, and it is not until a careful examination of the chest is undertaken that the presence of a cardiac murmur focuses attention on the heart as a possible cause of the symptoms. Evidence of some degree of cardiac decompensation, such as increase in venous pressure, hepatomegaly or obvious dyspnœa at rest, is very frequently present. When such signs are found, intensive medical therapy is commenced in order to resuscitate the child before operation, as has already been indicated. It is most unwise to proceed to immediate operation in these cases before controlling any degree of cardiac failure that is present with appropriate medical therapy. In general, no additional investigations, apart from routine X-ray examination of the chest, electrocardiograms and examination of the blood, are undertaken in these cases, as the children are usually seriously ill, and time spent on such procedures as angiocardiography or cardiac catheterization may well militate against the possibility of survival. We have always adopted the attitude that if a patent ductus cannot be reasonably excluded on clinical examination, these children should be submitted to exploratory thoracotomy, since, if a duct is present, its ligation may well prove a life-saving procedure, and little is lost if it is found that an intracardiac shunt is the cause of the failure to thrive. In practice, reliance on the peripheral signs and a careful appraisal of the clinical signs that are present will usually result in a correct diagnosis by an

experienced cardiologist. We are aware that in some overseas units extensive use has been made of retrograde aortography (Keith and Forsyth, 1950), and we have attempted it on a few occasions; but the results have, in general, been disappointing, and we hold that an accurate diagnosis is almost invariably possible on clinical grounds alone.

Complicated Patent Ductus.

Patent Ductus with Pulmonary Hypertension.

When any major degree of pulmonary hypertension is present in association with a patent ductus arteriosus, the clinical signs are profoundly altered, and the risks of operative interference become very materially increased (Kirklin *et alii*, 1955). With mild to moderate pulmonary hypertension (up to 70 or 80 mm. of mercury) there is little alteration in the physical signs. A continuous murmur is usually still present, and it is only the accentuation of the pulmonary second sound and the presence of a variable degree of right ventricular preponderance in the electrocardiogram that direct one's attention to the possibility that pumonary hypertension may be present. The X-ray film in such cases usually shows an appreciable degree of cardiomegaly, a marked accentuation of the pulmonary artery segment and a substantial increase in the pulmonary vascular markings, which sometimes tend to be less obvious in the peripheral third of the lung fields. However, these findings are more pronounced when the pulmonary hypertension is of marked degree. In these cases surgery should always be recommended, and it carries little, if any, increased risk. The ductus will invariably be found to be a large one, and if biopsy of the lingula is carried out at the time of thoracotomy, no changes in the lung vessels will be found to be present. Catheterization is carried out as a routine in such cases, to determine the degree of pulmonary hypertension and to confirm the diagnosis, and it will almost invariably be found that the catheter can be passed through the patent ductus. Recatheterization six to 12 months after operation constantly shows a substantial reduction in the pulmonary artery pressure in these cases, and there is good reason to believe that it returns to normal levels after the lapse of a year or so in virtually all cases.

When the pulmonary artery pressure is at or above systemic levels, a considerable difference of opinion exists as to whether any attempts should be made to close the ductus. In such cases the systolic murmur remains, but the diastolic element of the murmur is usually completely obliterated. There is a gross accentuation of the pulmonary second sound, and an ejection click is almost invariably present at the pulmonary area. Catheterization must always be undertaken in such cases, to determine the precise level of the pulmonary artery pressure and to ascertain whether the shunt of blood is still predominantly left to right or whether it has become bidirectional, as may be strongly suspected if there is any substantial increase in the hæmoglobin level. It is our practice to recommend operation in all such cases that are discovered in childhood.

At operation, pressure readings are taken in the pulmonary artery before and after occlusion of the ductus. If it is found that the pulmonary artery pressure increases after occlusion of the ductus, it is not ligated and the chest is closed. If, however, the pulmonary artery pressure remains the same or drops appreciably after occlusion of the duct, then the operation is proceeded with in the usual manner; either the duct is ligated, or, if it is very wide and short, it is transected and the two ends are oversewn. After operation, such patients are kept continuously in oxygen for at least a week, as it is thought that this guards to some extent against the development of a sudden increase in the pulmonary hypertension, with a possibility of acute failure of the right side of the heart. All these patients are given digitalis before operation, and digitalis therapy is continued for some considerable time after operation. Of course, operation in such cases may carry a substantial mortality; but in the limited number of such operations that we have performed, this would not appear to be prohibitive. After a successful operation, cyanosis disappears and the hæmoglobin value returns to normal levels. A sufficient number of these operations has not been done yet to determine whether a substantial and permanent reduction in the pulmonary artery pressure will result; but in some cases post-operative recatheterization after an interval of a year or so has been extremely gratifying.

Patent Ductus with Other Congenital Heart Lesion.

We have encountered a patent ductus in combination with almost every other congenital heart lesion. It is not infrequently seen in conjunction with a ventricular septal defect. We have on several occasions encountered it with an atrial septal defect. It is also present in some 20% of cases of coarctation of the aorta, and we have also seen it in conjunction with severe pulmonary stenosis, with fibroelastosis and with aortic stenosis. When patent ductus exists in conjunction with a ventricular septal defect, such patients frequently present in cardiac failure early in life. In such cases the ligation of the duct, even if it is a small one, will almost invariably produce a beneficial result, and the child will then commence to thrive, will become stabilized and will progress in spite of the presence of the ventricular septal defect. Patients with an atrial septal defect almost invariably present in cardiac failure early in life. Considerable care must be taken in preparation of such patients for operation, since they are very liable either to fibrillation during thoracotomy or to acute cardiac failure in the immediate post-operative period. In general, it will be found advisable to deal with the patent ductus arteriosus as a first procedure, and to defer any attempt at closure of the atrial septal defect for some considerable time. When patent ductus exists in conjunction with a coarctation, it is, of course, dealt with at the same time as the coarctation. When pulmonary stenosis or aortic stenosis is present, considerable judgement may be required to decide which of the two lesions is the more serious and which should be dealt with first. In the few cases that we have encountered, we have usually dealt with the more serious lesion as a first procedure, and have deferred operation on the less disabling of the two lesions until a subsequent date. When patent ductus occurs in conjunction with fibroelastosis, such patients present in acute heart failure early in infancy. After resuscitation of the patient the ductus should be closed, and, if this is feasible, a left atrial biopsy can be taken at the same time to confirm the diagnosis of fibroelastosis. It has been our experience that, after successful closure of the ductus in such cases, the fibroelastosis appears to regress, and the patient's condition may become clinically normal after the lapse of a few years.

Patent Ductus with a Non-Cardiac Lesion.

When a patient with a patent ductus presents with some other surgical lesion, in general the patent ductus should be dealt with prior to an attack on the other lesion, unless it is of an acute nature. In such cases, of course, surgery must be undertaken for the alternative lesion, and an antibiotic cover should always be given to guard against possible infection of the ductus in the post-operative period. This is another reason for dealing with a patent ductus early in life when its presence is known.

The Recurrent Ductus.

The recurrent ductus constitutes a special problem. When patency recurs, it invariably does so within a few months of operation, and in most cases in the immediate post-operative period. In some cases, recurrence is due to a fine ligature cutting through the ductus with the formation of a false aneurysm. However, it is most frequently due to the ligatures around the ductus not being tied tightly enough, so that the original ductus reforms early in the post-operative period. In such cases, the classical continuous murmur and the peripheral signs of a ductus quickly become manifest again. At re-operation, no particular difficulty is usually found in dealing with such a ductus apart from some reactive fibrosis in the area of the previous operation. In general, re-opera-

tion should be advised in these cases, as it can be carried out with very little additional risk and a complete cure can be produced.

The Infected Ductus.

Bacterial endocarditis or endarteritis is uncommon in the paediatric age group; but it can occur in association with the patent ductus, in which case the vegetations most commonly form at the pulmonary end of the ductus. In such cases, massive chemotherapy should be utilized to control the infection, after which closure of the ductus can be undertaken. In general, it is unwise to advise surgical closure during the phase of active endarteritis, when the tissues around the duct will be œdematous and the anatomy of the part is likely to be obscured, the ductus itself being friable and easily torn.

Results.

Uncomplicated Patent Ductus.

The total number of cases of uncomplicated ductus was 92. A cure was achieved in 91, recanalization did not occur, and there was one death (four months after operation).

This child developed staphylococcal pneumonia and empyæma on the fourth day after operation. This subsequently led to staphylococcal endarteritis in the vicinity of the ligated duct and staphylococcal septicæmia. The left pulmonary artery became aneurysmal, and communication with the aorta recurred, a continuous murmur reappearing about two month after operation. Death from hæmorrhage occurred during a further operative attempt to obliterate the aneurysm and close the communication with the aorta.

Complicated Patent Ductus.

The total number of cases of complicated patent ductus was 28. A cure was achieved in 23, thoractomy only was performed in two, three patients died, and in no case did recanalization occur.

One child who underwent thoracotomy only was operated on for what was presumed to be an uncomplicated classical patent ductus. However, at thoracotomy the aorta was found to be on the right side, and careful dissection of the left pulmonary artery failed to reveal any ductus. Subsequently a right thoracotomy revealed a right-sided patent ductus from the right pulmonary artery to the aorta, and this was accordingly ligated.

This "complicated" group includes the following: (i) a large patent ductus in infants admitted to hospital with congestive heart failure; (ii) patent ductus with severe pulmonary hypertension; (iii) patent ductus combined with another lesion (excluding coarctation), as follows: (a) ventricular septal defect, (b) atrial septal defect, (c) severe pulmonary stenosis.

The three fatal cases warrant special comment.

One patient was an infant, aged three months, in congestive cardiac failure, who had failed to thrive from birth. Her weight on her admission to hospital was 7·5 lb. She was resuscitated in the usual manner on medical therapy, and subsequently underwent ligation of a large ductus. After operation she became pyrexial, developed abdominal distension and frequently passed offensive stools. She failed to improve, and on the ninth day after operation her condition suddenly deteriorated further, and she died that evening. Post-mortem examination revealed a ligated ductus and a small ventricular septal defect. The left ventricle was grossly hypertrophied. There was evidence of bronchopneumona and septicæmia, which had apparently developed after operation because of her debilitated condition.

The second child was an infant, aged 21 months, weighing 19·5 lb., who had been in hospital six times in her short life with recurrent congestive cardiac failure and failure to thrive. Cardiac catheterization was carried out and confirmed the presence of an atrial septal defect, a large patent ductus and marked pulmonary hypertension, the pressure in the pulmonary artery being 80/40 mm. of mercury and that in the left ventricle 95/4 mm. of mercury. After considerable discussion it was decided to ligate the ductus. Fibrillation occurred while the chest was being closed, and a satisfactory cardiac action could not be reestablished.

The third death was that of an infant, aged three months, weighing 8 lb., who had been admitted to hospital with acute bronchopneumonia and congestive cardiac failure at the age of six weeks. After the infection and the cardiac failure had been controlled as adequately as possible, operation was undertaken and a large patent ductus was found and ligated. The child suddenly collapsed and died 20 hours later. Post mortem, the left lung was found to be collapsed and the right side of the heart was markedly dilated. A small ventricular septal defect was present, and the ductus was securely closed.

Discussion.

This series would appear to compare favourably with others reported (Gross, 1952; Robb, 1952). Many ligation techniques have fallen into disfavour because of the proportion of cases in which there has been a recurrence. However, there is no doubt that ligation is quicker and easier to perform, and when thick ligatures as described are used, the risk of cutting through the ductus is minimal and recurrence is very uncommon. Particularly in infants in incipient cardiac failure with a large ductus, it is thought that this technique has much to recommend it, since it can be carried out so expeditiously and with a minimum of dissection.

The axillary approach described could also be used more frequently and selectively than it is. Its advantages and limitations have, perhaps, not been fully appreciated to date. It has frequently been stated that the exposure obtained is inadequate, and this is true if it is used outside the correct age group. However, in children under the age of four years, the exposure is excellent if the incison is correctly made, and in infants is actually better than that afforded by a standard lateral thoracotomy. Moreover, in this age group a variety of procedures may be carried out through this incision (for example, repair of tracheo-œsophageal fistula, lobectomy). Virtually no muscles are cut when this approach is utilized, and the freedom from discomfort or constitutional disturbance in the immediate post-operative period is quite striking in these small patients, apart from the obvious cosmetic advantages obtained.

Operative closure of the patent ductus arteriosus is now so safe and uniformly satisfactory that there is no question but that it should be recommended whenever the lesion is diagnosed with certainty. In addition, there are definite dangers and disadvantages in procrastination, less disturbance is caused the earlier operation is carried out, and it is technically easier in infants than later in childhood. Therefore, the time of election for surgery is as soon as possible after the diagnosis has been established.

Summary.

A personal series of 120 cases of patent ductus arteriosus is discussed.

In 92 uncomplicated cases there was one death, and the remaining 91 patients have achieved a complete cure. It is suggested that the ligation technique described is safe and satisfactory. An axillary approach has much to recommend it in children under the age of four years, and surgery should be recommended in all cases as soon as a definite diagnosis has been established. In most cases this is possible on clinical grounds, without the necessity for any specialized investigations other than routine X-ray examination and electrocardiography.

A group of 28 cases of complicated patent ductus is presented, in which (i) infants presented in congestive cardiac failure with a patent ductus, (ii) severe pulmonary hypertension was present, (iii) another significant heart lesion was present in addition to a patent ductus.

References.

ADAMS, F. H., and FORSYTH, W. B. (1951), "The Effect of Surgery on the Growth of Patients with Patent Ductus Arteriosus", *J. Pediat.*, 39: 330.

BLALOCK, A. (1946), "Operative Closure of the Patent Ductus Arteriosus", *Surg. Gyneo. Obstet.*, 82: 113.

BROWNE, D. (1952), "Patent Ductus Arteriosus", *Proc. roy. Soc. Med.*, 45: 719.

CAMPBELL, M. (1952), "Patent Ductus Arteriosus", *Brit. Heart J.*, 17: 511.

CLAGETT, O. T., KIRKLIN, J. W., ELLIS, F. H., and COOLEY, J. C. (1955), "Surgical Treatment of Patent Ductus Arteriosus", *Surg. Clin. N. Amer.*, August: 965.
GROSS, R. E. (1947), "Complete Division for Patent Ductus Arteriosus", *J. thorac. Surg.*, 16: 314.
GROSS, R. E. (1952), "The Patent Ductus Arteriosus: Observations on Diagnosis and Therapy in 525 Surgically Treated Cases", *Amer. J. Med.*, 12: 472.
GROSS, R. E., EMERSON, P., and GREEN, H. (1940), "Surgical Obliteration of Patent Ductus Arteriosus in 7 Year Old Girl", *A.M.A. J. Dis. Child.*, 59: 554.
KEITH, J. D., and FORSYTH, C. (1950), "Aortography in Infants", *Circulation*, 2: 907.
POWELL, M. L. (1955), "Patent Ductus Arteriosus in Infancy with Gross Cardiac Embarrassment", MED. J. AUST., 1: 109.
ROBB, D., and NICKS, R. (1952), "The Surgical Treatment of Patent Ductus Arteriosus: A Report on Eighty-Two Cases", *N.Z. med. J.* 51: 31.
STUCKEY, D. (1957), "Palmar Pulsation: A Physical Sign of Patent Ductus Arteriosus in Infancy", MED. J. AUST., 2: 681.

MODERN CONCEPTS OF PLACENTA PRÆVIA.

By L. WOODROW COX,
From the Department of Obstetrics and Gynæcology,
University of Adelaide.

THE diagnosis and management of cases of placenta prævia have been well-documented by many authors in recent years. Those who have contributed most to the literature on this subject are Marshall (1939), for his championship of the lower segment operation in placenta prævia, Macafee (1945) and Johnson (1945), for their concept and practice of expectant treatment, and Stallworthy (1951), for his careful observations on the management of this disorder. A number of basic principles are often neglected, particularly the clinical history and clinical observations on patients with placenta prævia. A very careful clinical assessment of each case very often leads to a presumptive diagnosis which is so strong that further evidence can be regarded as only confirmatory.

The Clinical History of Placenta Prævia.

Bleeding is the first sign in the majority of cases of placenta prævia. The amount of this first loss may be slight—just a stain, which is passed over by both patient and attendant. However, this stain is the first separation

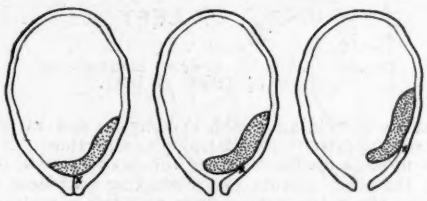


FIGURE I.
The lower segment taking up. Diagram showing the change in shape of the lower uterine segment and cervix near to term. The *internal os is marked X.*

of the placenta prævia from the lower uterine segment, and it may occur at any stage of pregnancy, even in the early months.

Usually the first hæmorrhage comes when the cervix begins to take up—that is, at some time after the thirtieth week of gestation. It is reasonably certain that this bleeding will stop, but that it will inevitably recur. It may recur soon or late, and when it does, the loss will be heavier than on the previous occasion. The bleeding will also stop on these later occasions unless labour begins, when the blood loss continues until delivery is complete.

It is this recurrence of bleeding, with more severe loss each time, which is the most important feature of placenta prævia, both from the diagnostic and therapeutic standpoints. The initial "show" matters little—the patient is not endangered. The second time, the amount of blood lost may be a pint, while third and subsequent hæmorrhages almost invariably endanger the patient's life.

When labour begins, as the cervix dilates, one expects the greatest alteration in the respective shapes of placenta and uterine wall. With a central placenta prævia, considerable separation of the placenta occurs. The non-central type may remain fairly well applied to its insertion,

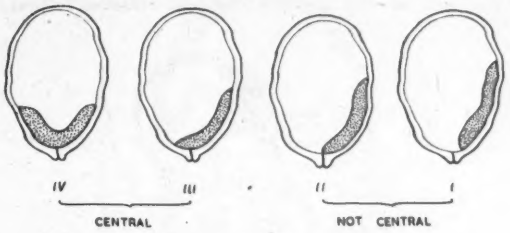


FIGURE II.
The types of placenta prævia. "Central" includes *Types III and IV.*

but as the lower border must be separated a little, steady blood loss continues throughout labour. This bleeding occurs between uterine contractions, when the uterine muscle is relaxed and the blood flows more freely through the uterine sinuses. It is usually a steady trickle, except for slight stoppages during uterine contractions. Although the rate of bleeding may appear slight, its continuance over several hours of labour may lead to grave exsanguination. When the child is delivered, bleeding does not stop

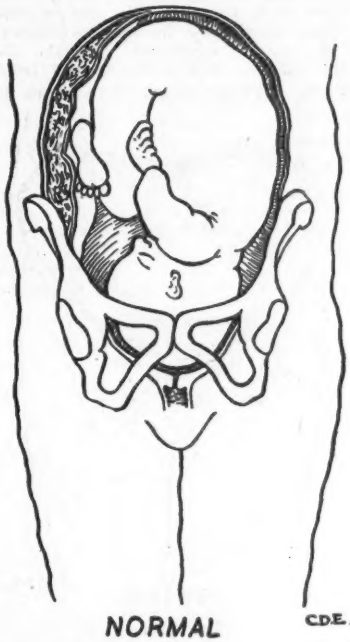


FIGURE III.
The normally inserted placenta, with the fœtal head engaged in the pelvis.

until separation and expulsion of the placenta are complete. Retraction of the lower segment occurs quite strongly, although the muscle is not as thick as it is in the upper segment, and bleeding is controlled when the uterus is empty.

In parenthesis, at this point let me mention that in central placenta prævia there is sometimes no separation

of the placenta at all—that is, no bleeding occurs in the ante-natal period. The placenta prævia is discovered only at Cæsarean section for "disproportion", or when labour begins with bleeding, or in some other way.

The Clinical Examination of the Patient.

There are two important features that may be observed, and the discovery of these features, added to the history of the case, usually provides sufficient evidence to make a

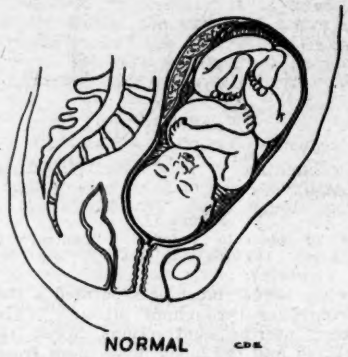


FIGURE IV.
Sagittal view of a normally inserted placenta with engaged head.

diagnosis of placenta prævia. The first feature is flaccidity of the uterine and abdominal muscles. When bleeding begins, in most cases the patient is not in labour, so the usual non-contracted state of the uterine muscle is present. Very little placenta is separated from the uterine wall, and the blood that is shed is discharged freely through the internal os. There is no increase in intrauterine

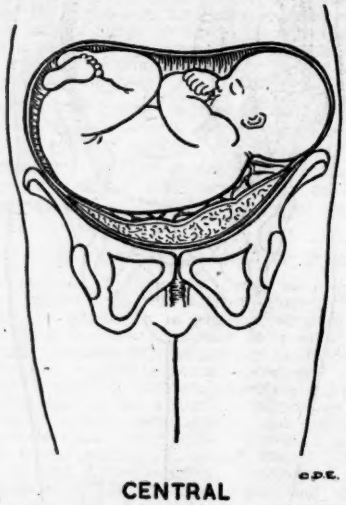


FIGURE V.
Central placenta prævia prevents either pole of the fœtus from entering the pelvic brim. The lie is transverse.

pressure, either in a local area of placental site, or generally throughout the whole uterine cavity, so the uterus is not stimulated to contract. As the bleeding continues and the effect of blood loss on the whole body is apparent, the voluntary muscle tone seems lower. The result is that there is less resistance to palpation of the uterus, and fœtal parts are often more clearly felt than usual.

The second and most important feature of all is that of malpresentation. I use this word deliberately. It is strictly true, although many do not realize it. The malpresentation may be small or large, but it is almost invariably present at some stage, when the diagnosis of placenta prævia can be made. In a normal pregnancy, the presenting part engages the pelvic brim. However, when there is a central placenta prævia, the fœtus often lies transversely or obliquely, because the placenta prevents either pole from entering the pelvis. Much more commonly, the degree of malpresentation is small, and the casual observer will not pay sufficient attention to it. When the placenta is inserted on the left or right side of the lower segment, the presenting part is not centrally situated, and appears to override the pelvic brim on the opposite side. This is usually noticed even if the full significance is not recognized. When the placenta is on the posterior wall, the presenting part is pushed forwards.

FIGURE VI.
Central placenta prævia causing an oblique lie (right or left).

This causes overriding of the symphysis, and in cephalic presentations falsely simulates disproportion. Usually there is upward displacement of the head as well, so that even in the erect posture the presenting part does not fit down onto the pelvic brim. This really is a malpresentation, although at first one may not think so.

When the placenta is on the anterior wall, the observer is very easily confused. The thick placenta lies beneath the abdominal wall, and in front of the presenting part. The fœtal outlines are blurred, if they can be felt at all. The most common error is to think one feels a breech, when actually it is the head which is obscured by placenta.

The abdominal examination is of the utmost importance. Near term, in the average-sized patient, there is not room in the pelvis for both placenta and presenting part, either head or breech. Therefore, a malpresentation is produced. The observation of this, together with a clear interpretation of the history of recurrent bleeding, is strong presumptive evidence of placenta prævia. The presence of a transverse lie, together with a major hæmorrhage from a soft uterus, is quite certainly diagnostic of a central placenta prævia.

There are, however, cases which do not conform to this pattern. When the fœtus is small and the mother has a large pelvis, there may be room in the pelvis for both

placenta and fœtal head, particularly in certain non-central Type I and Type II cases. Here one may expect a safe spontaneous labour, with a minimum of bleeding, and until term is reached and labour begins, the diagnosis often remains uncertain. On the other hand, in normal cases

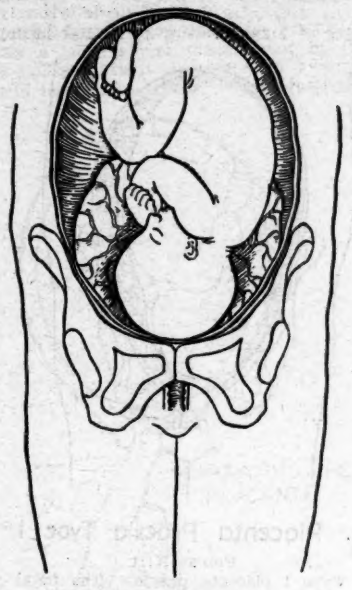


FIGURE VII.
Placenta prævia inserted on the posterior wall. The fœtal head is prominent.

several weeks before term, it is not uncommon for temporary malpresentations to occur, and if bleeding from some other cause is revealed at that time, placenta prævia may be falsely diagnosed.

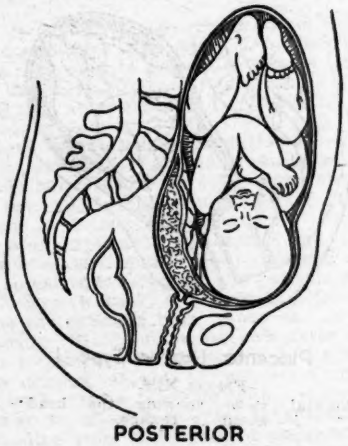


FIGURE VIII.
Posterior placenta prævia simulating disproportion.

I have laboured these points of clinical diagnosis, because I am sure they are being forgotten, and I make no apology for doing so. I am quite certain that in the majority of cases, a careful history, together with the abdominal findings, will lead to a confident diagnosis. Marshall (1939) stated that these points form a chain of circumstantial evidence that puts the issue beyond all reasonable *doubt.*

X-Ray Confirmation.

To confirm this presumptive diagnosis may not be so easy. The clinician is greatly in debt for the X-ray techniques of Reid (1949), Whitehead (1953) and Hartley

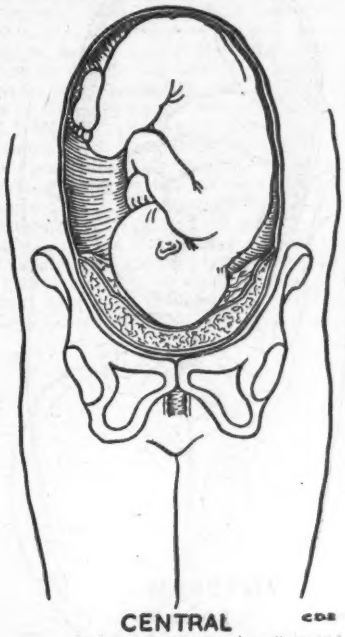


FIGURE IX.
Central placenta prævia, showing that the head does not approach the pelvic brim, even in the erect posture.

(1954). The evidence of soft-tissue radiography is most valuable, but it is only confirmatory of what should have been deduced already—namely, the existence and location of a placenta prævia. Thanks to these workers, and to their predecessors Snow and Powell (1934) and Dippel

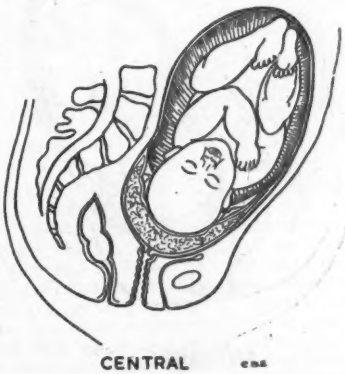


FIGURE X.
Sagittal view, showing failure of the head to engage.

and Brown (1940), there is now great accuracy in this field. Especially valuable is radiographic confirmation of the placenta prævia that is only suspected and not even deduced—that is, when there is a persistent high malpresentation without the occurrence of bleeding.

Vaginal Examination.

Vaginal examination is the only other practical method of confirming the diagnosis. For many years now teachers of obstetrics have instructed their students not to

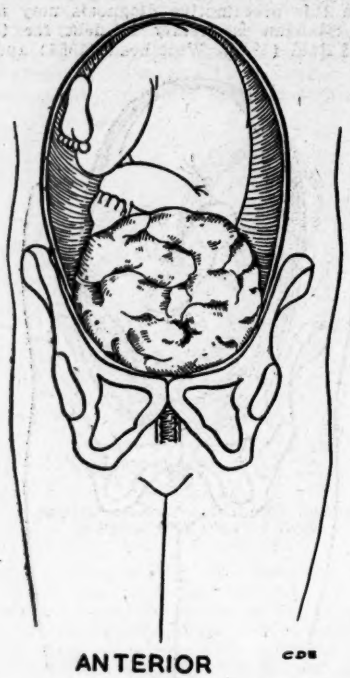


FIGURE XI.

Anterior placenta prævia; the placenta obscures the presenting part.

examine vaginally patients who have ante-partum hæmorrhage in case there is a placenta prævia. This is good advice.

While, in general, more mistakes are made by those who do not examine patients than by those who do, the vaginal

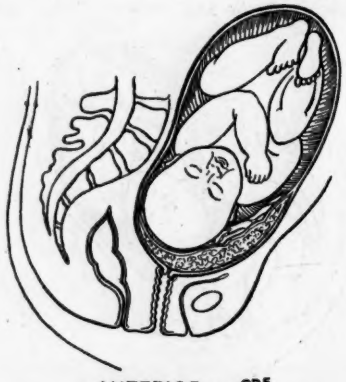


FIGURE XII.

Sagittal view of anterior placenta prævia.

examination in cases of placenta prævia is an exception. If the os is closed, and one must judge the presence or absence of a placenta prævia by the thickness of the tissues felt through the fornix, one is easily mistaken. If the os is closed and one forces the examining finger through it, to obtain a precise diagnosis, one inevitably separates placenta in every case of placenta prævia. Further, in the minor degrees, one may rupture the marginal sinus and produce torrential hæmorrhage. The only occasion on which one will do no harm is when the ante-partum hæmorrhage is not due to placenta prævia. Even here, the diagnosis may be made wrongly, because in many cases of long-standing accidental hæmorrhage of

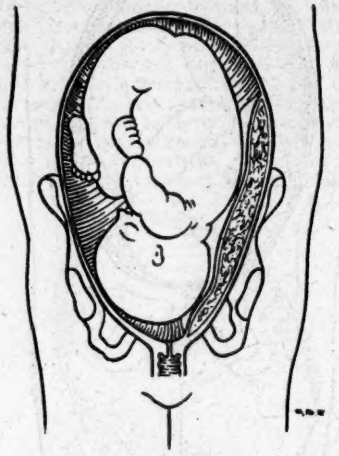


FIGURE XIII.

Type I placenta prævia. The fœtal head is entering the pelvis beside the placenta.

minor degree, the bag of forewaters becomes covered with a shaggy fibrinous covering, which is very like placental surface to feel. So it may happen that the vaginal examiner may actually make a wrong diagnosis because of his passion for precision.

The time for vaginal examination in placenta prævia, and the only time, is when the patient is in labour and is bleeding, and either the decision whether to allow labour

FIGURE XIV.

Sagittal view, showing the head about to engage.

to proceed or whether to perform Cæsarean section cannot be made on the other evidence, or it is likely that puncture of the forewaters may help the progress of labour. There is no justification for the "elective" vaginal examination when the patient is not bleeding, is at rest in the ante-natal ward and is, in fact, in no immediate danger whatever.

If one sifts the evidence carefully, one can proceed confidently to Cæsarean section without vaginal examination

in 90% of cases presumed to be of central placenta prævia (Types III and IV). The diagnosis is confirmed at operation. On the other hand, one may never confirm the diagnosis of a Type I placenta prævia, because the patient delivers her child past the placenta without undergoing a vaginal examination prior to delivery.

Management of the Patient.

The patient suspected of placenta prævia should be examined by a professional obstetrician at the earliest opportunity. The patient presumed to have a placenta prævia should be admitted to a proper maternity hospital

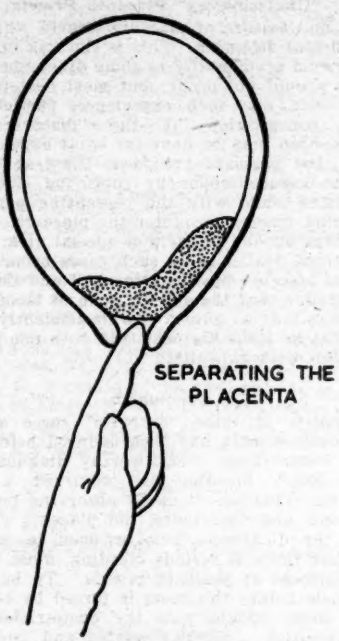


FIGURE XV.
The vaginal examination causes separation of the placenta.

with all facilities. Blood, cross-matched for the patient, should be available. The object of treatment should be to allow the pregnancy to proceed as near to term as practicable, so that a mature infant is produced. This waiting treatment, so ably expounded by Macafee (1945, 1946, 1950) and by Johnson (1945, 1950), runs the risk that serious hæmorrhage may occur during the waiting period. This is a calculated risk, and is worth while. Macafee (1945) and others make the point that waiting just a few days is not expectant treatment. Grant (1955) sets out the routine at Belfast quite succinctly. Until the thirty-seventh week expectant treatment is practised, unless a sudden severe hæmorrhage following several small episodes compels operative interference. In patients admitted after the thirty-seventh week, treatment is deferred merely to determine the patient's blood group and to examine her radiologically. Most authorities now agree that once the diagnosis of central placenta prævia is confirmed, elective Cæsarean section should be performed at the thirty-seventh week. Other patients with non-central placenta prævia may be allowed to start in spontaneous labour; slight bleeding from the separated placental site may be controlled, and the delivery may be hastened by rupturing the membranes during labour.

During the waiting or expectant period while the patient is in hospital, it is important that the patient's hæmoglobin value should be checked repeatedly and blood transfusion undertaken if the value falls below 12 grammes per 100 ml. It will be appreciated that profound fœtal anoxia will occur if there is a sudden hæmorrhage from a patient who is already anæmic. Not enough emphasis is given to this aspect of expectant treatment, possibly because the bleeding on each occasion is not severe or dangerous. The continual drain on the patient has its effect on the oxygen-carrying capacity of the blood. Also, the diminished area of placental surface for interchange resulting from the partial separation of the placenta is another factor with harmful effect on the fœtus.

I have observed, on more than one occasion, that the fœtal heart becomes faint, and even becomes inaudible, when the mother suffers a severe hæmorrhage. When she has been given a transfusion and is reviving, the fœtal heart is heard again, and gradually regains its normal strength during the next few hours. Because of this, I believe that operative interference in cases of severe hæmorrhage should be immediate, before the function of the fœtal heart is gravely impaired, or else delayed for many hours until resuscitation is complete. Such a regime is a counsel of perfection; but it is surprising how often an immediate operation can be carried out, provided that the patient's hæmoglobin level is normal before the sudden bleeding. In this respect one must reiterate the statement of one of our most recent visitors from overseas, that good obstetrics can be practised only with the Cæsarean operating room next door to the labour room. If the patient has to be transferred to another part of a hospital, the chance of immediate section is often lost.

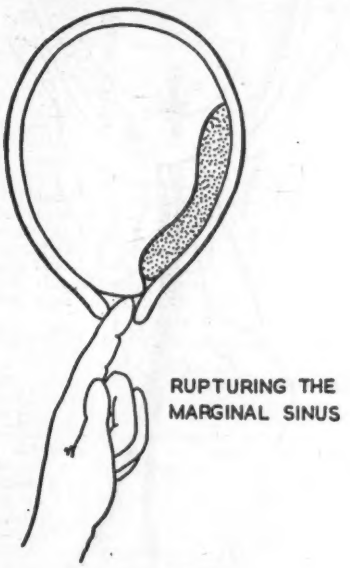


FIGURE XVI.
The marginal sinus may be ruptured in Type I cases.

Cæsarean Section.

The technique of operation in these cases should not differ from the standard one, so well illustrated in Marshall's book (1939). The lower-segment operation so far outweighs the classical operation in every respect, for safety to mother and fœtus (Marshall and Cox, 1950), that admitting no compromise, this discussion is confined to the lower segment operation. There is one important adjuration, however—there should be no panic when bleeding is free when the lower segment is opened; the operation must continue without any attempt to stop the bleeding until the fœtus has been extracted. Maternal lives are lost by vain attempts to stop large bleeding sinuses before extracting the child.

Marshall demonstrated an easy way of opening the uterus, which is useful in all placenta prævia cases and particularly in anterior wall placenta prævia. He pressed the fœtus upwards away from the pelvis, made a stab

wound through the lower segment, and then inserted one finger of each hand through this hole and stretched the wound laterally. This is quick, sure and effective. There is less bleeding, and the placenta can, if required, be separated before the child is extracted. It avoids cutting into placental tissue, and also blind snipping with scissors in a pool of blood, to open the lower segment. According to Neligan and Russell (1954), fœtal hæmorrhage from incisions in the placenta can be serious, hence this technique is even more valuable.

Ergometrine given intravenously as the child is extracted aids contraction of the uterus, and stops blood loss even from the large sinuses in the lower segment.

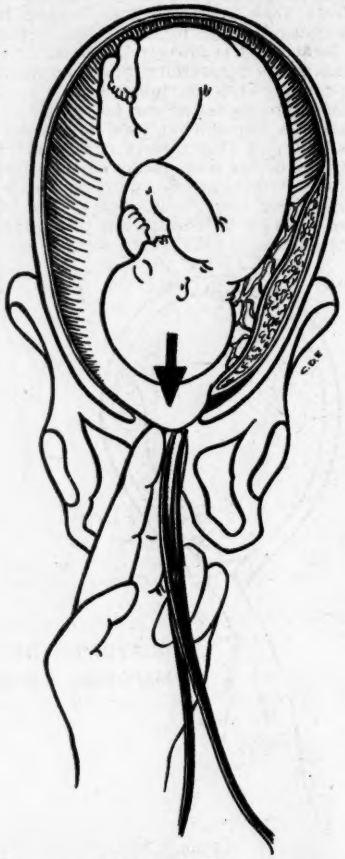


FIGURE XVII.
Artificial rupture of the membranes allows descent of the head, and pressure on the separated placenta.

Green-Armytage forceps control the few large bleeding vessels at the cut edge, and the conclusion of the operation proceeds with a comparatively bloodless field.

It is probable that the scope of Cæsarean section should be widened in placenta prævia. The realization that fœtal anoxia is a grave risk even in Type I and Type II cases, and particularly those in which the placenta is situated posteriorly (Stallworthy, 1951), leads many to suggest that the occurrence of severe bleeding (even if it has stopped) should lead to serious consideration of abdominal delivery (Moir, 1956). The fœtal salvage rate is higher, and, in Belfast, has reached the peak of nearly 90%—that is, 11% mortality (Grant, 1955). In Dunedin, too, the fœtal mortality rate was eight out of 73 cases (11%, 1951-1957), with 77% Cæsarean sections. The mortality in all cases was due to prematurity when expectant treatment failed (Wright, 1959).

Other Methods.

The older methods of delivery are now in the discard. Bipolar version, Willett's forceps and hydrostatic bags belong to another era, the only exceptions being when the fœtus is dead, malformed, or previable, or perchance as treatment of desperation in emergency far from the well-equipped clinic. There is no need to consider methods with a fœtal mortality rate of 50% to 80% and a maternal mortality rate from 1% to 5% when results such as those of Macafee and Grant (1955), Johnson (1950), Stallworthy (1951), Mills (1948) and even our own are on record.

"Undiscovered" Placenta Prævia.

There is one feature of placenta prævia which does not receive sufficient attention. This is the risk of discovering placenta prævia accidentally at some other obstetric operation. This should not occur; but most obstetricians have had more than one such experience, particularly when called in consultation by the "discovering" party. Cæsarean section may be done for what appears to be disproportion, but placenta prævia is the true abnormality. Attempts to induce labour by rupturing the membranes are sometimes made with the presenting part high, and the examining fingers encounter the placenta. The first of these mishaps appear to carry a special risk, there being three maternal deaths in 42 such cases occurring in over 800 cases of placenta prævia (Marshall and Cox, 1950). It appears possible that the sudden gush of blood under such circumstances may so unnerve an insufficiently experienced operator that he loses his head and does not proceed with the operation with expedition.

Conclusion.

The opposite of these "surprise" cases are those in which placenta prævia has been deduced before there has been any hæmorrhage. Stallworthy diagnosed 16·5% of his cases before bleeding had occurred, a remarkable achievement. This was done by observing persistent malpresentations, and visualizing the placenta radiologically. To make the diagnosis thus, or even to make it with surety before there is serious bleeding, must be the object in the treatment of placenta prævia. To be confident of the diagnosis before the issue is forced by severe hæmorrhage or fœtal anoxia puts the obstetrician in a commanding position. He can advise and perform section immediately any bleeding begins, with far superior results for the fœtus. Once the thirty-seventh week has been reached during expectant treatment, if the diagnosis is certain, elective section before a crisis occurs is undoubtedly the treatment of choice.

The "deduction" of the presence of placenta prævia is probably the most important factor in the modern management of the condition. It is important to the professional obstetrician in the city hospital; it is more important to the lone practitioner in the country. To the latter, his attendance at a case of placenta prævia is a nightmare—no stored blood for transfusion, no colleague for consultation or help with an operation. To deduce the presence of a placenta prævia and to send the patient safely to a base hospital before dangerous bleeding has threatened her life must be his object. To recognize the significance of malpresentations with, and even without, some bleeding will lead to much improved results in the treatment of placenta prævia.

Acknowledgement.

My thanks are due to Miss C. D. Entwhistle, Medical Illustrator, University of Otago Medical School, for the diagrams.

References.

DIPPEL, A. L., and BROWN, W. H. (1940), "Roentgen Visualization of the Placenta by Soft Tissue Technique", *Amer. J. Obstet. Gynec.*, 40: 986.

GRANT, F. G. (1955), "Placenta Prævia: A Review of 200 Cases", *J. Obstet. Gynæc. Brit. Emp.*, 62: 497.

HARTLEY, B. (1954), "Incidence and Significance of Placental Calcification", *Brit. J. Radiol.*, 27: 365.

JOHNSON, H. W. (1945), "The Conservative Management of Some Varieties of Placenta Prævia", *Amer. J. Obstet. Gynec.*, 50: 248.

JOHNSON, H. W. (1950), "The Management of Placenta Prævia", *Amer. J. Obstet. Gynec.*, 59: 1236.

MACAFEE, C. H. G. (1945), "Placenta Prævia: A Study of 174 Cases", *J. Obstet. Gynæc. Brit. Emp.*, 52: 313.

MACAFEE, C. H. G. (1946), Discussion on "Placenta Prævia", *Proc. roy. Soc. Med.*, 39: 551.

MACAFEE, C. H. G. (1950), "Modern Trends in Obstetrics and Gynæcology", Butterworth, London.

MARSHALL, C. M. (1939), "Cæsarean Section Lower Segment Operation", Bristol.

MARSHALL, C. M. (1951), Discussion on "New Ideas about the Diagnosis and Treatment of Placenta Prævia", *Proc. roy. Soc. Med.*, 44: 127.

MARSHALL, C. M., and COX, L. W. (1950), "The Results of a Collective Investigation into Cæsarean Section (1943-1947) Made for the 12th British Congress of Obstetrics and Gynæcology", "Transactions of the XIIth British Congress of Obstetrics and Gynæcology", London.

MILLS, W. G. (1948), "The Conservative Treatment of Placenta Prævia", *Brit. med J.*, 2: 896.

MOIR, J. C. (1956), "Operative Obstetrics", Baillière, Tindall & Cox, London.

NELIGAN, G. A., and RUSSELL, J. K. (1954), "Blood Loss from the Fœtal Circulation: A Hazard of Lower Segment Cæsarean Section in Cases of Placenta Prævia", *J. Obstet. Gynæc. Brit. Emp.*, 61: 206.

REID, F. (1949), "The Radiological Localisation of the Placental Site", *Brit. J. Radiol.*, 22: 557, 643.

SNOW, W., and POWELL, C. B. (1934), "Roentgen Visualization of the Placenta", *Amer. J. Roentgenol.*, 31: 37.

STALLWORTHY, J. A. (1951), "The Dangerous Placenta", *Amer. J. Obstet. Gynec.*, 61: 720.

STALLWORTHY, J. A. (1951), Discussion on "New Ideas about the Diagnosis and Treatment of Placenta Prævia", *Proc. roy. Soc. Med.*, 44: 121.

WHITEHEAD, A. S. (1953), "The Position of the Fœtus in Relation to Placental Site", *J. Obstet. Gynæc. Brit. Emp.*, 60: 854.

WRIGHT, J. L. (1959), "The Modern Management of Placenta Prævia", *N.Z. med. J.*, 58: 559.

DEMONSTRATION OF THE SO-CALLED BILE CANALICULI.

By E. B. JONES,
Prince Henry Hospital, Sydney.

DURING a study of various methods for the silver impregnation of reticulum in the liver, a simple and rapid procedure has been devised for the demonstration of the so-called bile canaliculi.

Method.

Solutions and Reagents.

Analytical reagent chemicals are used. Water used as a reagent is glass distilled. "Alcohol" is synonymous with "ethanol".

***Ammoniacal Silver Carbonate Solution (Foot[1]).*—To make this solution, 200 ml. of 5% anhydrous sodium carbonate solution are added to 50 ml. of 10% silver nitrate solution. The precipitate is allowed to settle, the supernatant fluid is poured off and the precipitate is washed six or seven times in distilled water. Very slowly, ammonia (sp. gr. 0·88) is added to the precipitate. The mixture is shaken, and the ammonia is continually added until the precipitate is dissolved. A deposit of metallic silver will generally be present. The solution can be decanted off and kept in a Coplin jar painted on the outside to exclude light. A fresh solution is made up every week, and is kept in the bath at 37° C. when in use.**

***Sodium Thiosulphate.*—Three hundred millilitres of a 5% solution of $Na_2S_2O_3.5H_2O$ are made each week and kept in a stoppered dark bottle, 50 to 60 ml. being taken each day and kept in a Coplin jar painted on the outside to exclude light.**

***Gold Chloride.* — One gramme of gold chloride ($HAuCl_4.xH_2O$) is dissolved in 100 ml. of distilled water and made up as a 0·5% solution in distilled water for use.**

[1] Described by Carleton (1946).

***Iodine Solution.*—The iodine solution is made up as follows: iodine, 12·5 grammes; potassium iodide, 3·0 grammes; absolute alcohol, 350 ml.; distilled water, 150 ml. Approximately 70 ml. of this solution are kept in a Coplin jar, and replaced each month.**

***Reducing Solution.*—One millilitre of formalin (formaldehyde 37% w/v) is made up to 100 ml. with distilled water. This solution is made up daily, and is kept in a stoppered dark bottle.**

***Citric Acid Solution—Stock.*—One gramme of citric acid ($C_6H_8O_7.H_2O$) is dissolved in 100 ml. of distilled water. This is stock solution, and is made up weekly.**

***Citric Acid Reagent for Daily Use.*—Five millilitres of citric acid stock reagent are made up to 50 ml. with distilled water to give a 0·1% solution. Acid formalin solution is composed as follows: citric acid solution (0·1%), 0·5 ml.; reducing solution, 5·0 ml.; tap water to 50 ml. This solution is placed in a Coplin jar and used for treating one slide only.**

***Fixatives.*—Formol saline fixative is made up as follows: formalin (formaldehyde 37% w/v), 100 ml.; sodium chloride, 8·5 grammes; tap water to 1 litre. Ferric chloride-formol saline fixative is prepared by adding two grammes of ferric chloride ($FeCl_3.6H_2O$) to 100 ml. of formol saline fixative.**

Method of Staining for Bile Canaliculi.

Sections of liver tissue approximately 0·5 cm. in thickness are fixed in formol saline for 72 hours and carried through the usual procedures to a paraffin section.

The paraffin section is brought to 70% alcohol in the usual manner, and then placed in the iodine solution for five minutes, then back through 70% and 50% alcohol and distilled water, then flooded with ammoniacal silver carbonate solution for one minute, then through two changes of distilled water for half a minute; it is placed in 50 ml. of acid formalin solution for one minute and then in distilled water for half a minute. The slide is then flooded with 0·5% gold chloride solution for three minutes, is passed through distilled water, and then placed in 5% thiosulphate solution for two minutes; after this it is passed through distilled water, blotted, dried carefully over a flame, flooded with methyl benzoate, blotted dry, placed in xylol and then mounted. The slide may be counter-stained with van Gieson's stain for three seconds after being treated with thiosulphate and washed.

Method of Staining Reticulum in Liver.

Sections of liver tissue no more than 0·5 cm. in thickness are fixed in ferric chloride formol-saline solution for 72 hours. Paraffin slides are then brought to water and placed in a Coplin jar containing ammoniacal silver carbonate solution at 37° C. for 30 minutes, then passed through two changes of distilled water for half a minute and then placed in 50 ml. of acid formalin solution for one minute and in distilled water for half a minute. The subsequent procedure is as given in the method for bile canaliculi. In both procedures it is essential that fixation be adequate, and that tissue be fixed as soon as possible after death. Biopsy material gives excellent results.

Results.

Stain for Bile Canaliculi.

The structures between the liver cells conform to the usual arrangement shown in diagrams of bile canaliculi. These intercellular structures cannot be demonstrated in such organs as the kindney or pancreas. In the guinea-pig liver, intercellular structures similar to those seen in human liver can be demonstrated. This intercellular material varies little in calibre, is often beaded in outline, does not form into larger channels, is uniformly distributed and follows the line of adjacent cell faces.

In areas of acute necrosis, as in infectious hepatitis, the former cell outlines are often delineated by the contents of the spaces that have stained.

It has been noted that in acute toxic conditions such as staphylococcal pneumonia, and in fatty degeneration of the liver, in which there may be compression of the sinusoidal spaces from swelling of liver cells—as can be seen in hæmatoxylin and eosin stained sections—the cell outlines are clearly shown by the black silver-precipitated material between cells when silver impregnation staining has been used.

TABLE I.

Subject Number.	Sex and Age in Years.	Hours After Death.	Bile Canaliculi.	Reticulum.	Liver Weight.	Jaundice.	Bilirubin.[1]	Comment on Sections Illustrated.
7397	M.: 26	4	Numerous.	Normal.	lb. oz. —	None.	—	Normal liver. Male aged 26 years, killed instantly. Note the regular pattern of the bile canaliculi, and the dense reticulum shown in the reticular stain. Figures I and II.
7126	M.: 49	14	Numerous.	Moderate amount.	2 1	Deep.	P. 4·0 T. 16·3	Infectious hepatitis. Sections show numerous bile canaliculi; in many areas liver cells have disappeared, but the canaliculi are outlined where cells have been present. The reticulum has a somewhat frayed appearance and is diminished in amount. Figures III and IV.
7213	M.: 48	30	Very occasional.	Diminished in lobules.	5 2	None.	P. 1·3 T. 3·0	Portal cirrhosis. Note the very occasional bile canaliculi; clinically the patient was not jaundiced. Though the lobules were surrounded by fairly dense connective tissue, there is only a scanty amount of reticulum around the parenchymal cells. Figures V and VI.
6916	M.: 68	53	Very occasional.	Diminished.	5 10	None.	—	Chronic venous congestion. Note the long time of fixation of tissue after death. Similar results have been found in such cases when fixation was carried out shortly after death. Canaliculi are very occasional, the reticulum framework is scanty, and the sinusoids are dilated with blood. Figures VII and VIII.

[1] P, prompt; T, total.

In such conditions as portal cirrhosis or diffuse hepatic fibrosis and chronic venous congestion, in which the normal arrangement of liver cords is generally lost, these intercellular structures are only occasionally seen, and then only where sufficient liver cells are in anatomical relationship. In severe chronic venous congestion, long tenuous chains of liver cells can be seen surrounded by lakes of blood.

Stain for Reticulum.

Fixation in formalin-ferric chloride solution preserves the parenchyma and shows clearly the relation of the liver cells to the reticulum framework. The reticulum fibres are thin regular linear structures, they form an intricate scaffolding for liver cells, they line the sinusoids, and generally a tangle of short wavy processes lies over the cells; the reticulum framework is never in the nature of an investing membrane. Figures II, IV, VI and VIII[1] show the variability of the reticulum structures; in chronic venous congestion the reticulum has largely disappeared.

Discussion.

Blood from the hepatic artery and portal vein passes into a liver lobule; it then courses through the liver sinusoids and is discharged through the central vein. It follows that a positive-pressure gradient exists, passing from the periphery of the lobule to its centre.

Again, the relation of the liver trabeculæ to the sinusoidal blood spaces is important. In "Schafer's Essentials of Histology" (1946) the following statement is made:

> Into these sinusoidal blood spaces, the walls of which are formed of only a single layer of endothelial cells, the tissue elements of the organ grow, invaginating the thin wall and forming cell trabeculæ within the sinus so that the cells of the organ are brought directly into contact with the invaginated endothelium, and are separated only by this from the blood contained within the sinus. But the connexion may be yet closer than this, for, as happens in the liver, the invaginated endothelium may largely disappear, so that the blood within the sinus is in actual contact with the cells of the organ, flowing in the irregular interstices between them.

Other authorities are in accord with this statement. The liver parenchymal cells have not developed any obvious anatomical structures related to their function, in contrast, for example, to the cells of the proximal convoluted tubules of the kidney. As Maximov and Bloom (1939) state:

> In spite of the manifold functions which the liver cells perform, there is a marked similarity in appearance in all of them. This is at variance with what is seen in other organs, in which highly specialized functions are carried on by cells which morphologically are highly differentiated.

It is generally agreed that free bilirubin is brought to the liver by the blood-stream, and is converted there by the parenchymal cells to bilirubin conjugates. From here the problem is, how does the conjugated bilirubin arrive in the bile ducts?

At the present time opinion varies as to the precise structure of the so-called bile canalicular system, as well as to its function as a collecting system. For many years injection methods of demonstrating the bile canaliculi have been regarded as final; but in spite of this being apparently the obvious method of demonstrating these structures, there appear to be no satisfactory histological preparations that show unequivocally the continuity of bile canaliculi to bile ducts. Whilst this is not proof of their absence, it must also be admitted that artefacts can easily be produced when material is introduced under pressure.

However, the work of Ahrens *et alii* (1951) showed that embryologically the bile ducts and liver parenchyma arise from separate *Anlagen*, and this is consistent with Andrews's (1955) view:

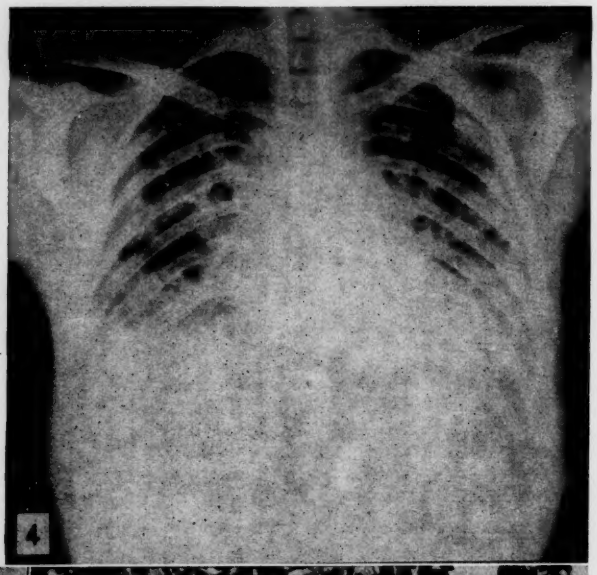
> . . . published observations on the excretory function of the liver support the hypothesis that the biliary tract secretes most if not all of the constituents of bile. This hypothesis entails a different concept of the functions of the parenchyma and biliary cells, but not of the reticulo-endothelium.

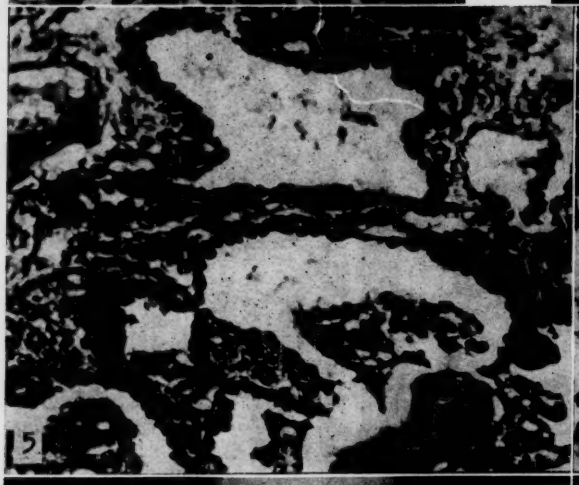
If the biliary epithelium is regarded as having a secretory function, analogies can be made with other systems in the body. Thus the adrenal cortex formulates various steroids as required by body metabolism, and having served their purpose they are transported to the liver by the blood-stream, conjugated and passed to the blood-stream and excreted by the kidneys. Similarly it could be inferred that bilirubin is formed in the reticulo-endothelial system, passed by the blood-stream to the liver and conjugated, and that the conjugates are excreted into the blood-stream and then secreted from the blood-stream by the biliary epithelium. It may also be suggested that the bile ducts occur in the liver only as a matter of anatomical convenience, and may possibly be regarded as functionally independent from liver cells. This intimate anatomical association of quite differently functioning tissues is not uncommon in the body, as witness the medulla and cortex of the adrenals, the thyroid and parathyroids, and the anterior and posterior lobes of the pituitary, each elaborating hormones with different physiological action.

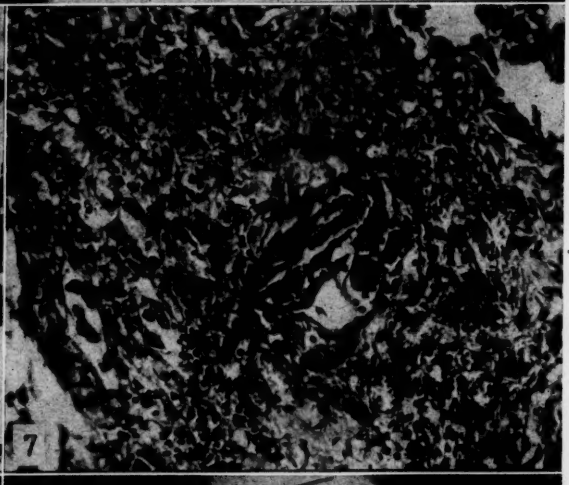
[1] For Figures I to VIII see art-paper supplement.

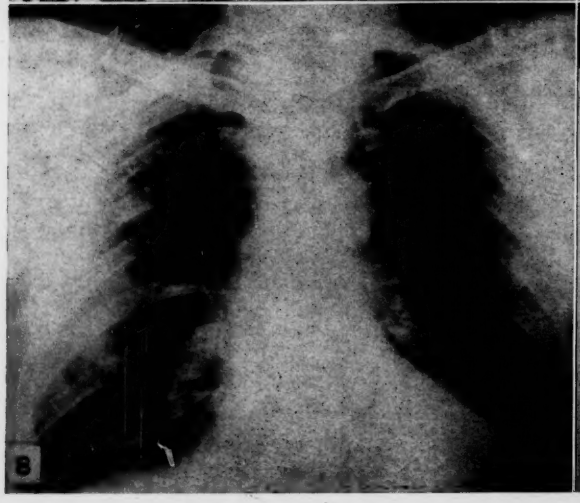
ILLUSTRATIONS TO THE ARTICLE BY JOHN BEVERIDGE.

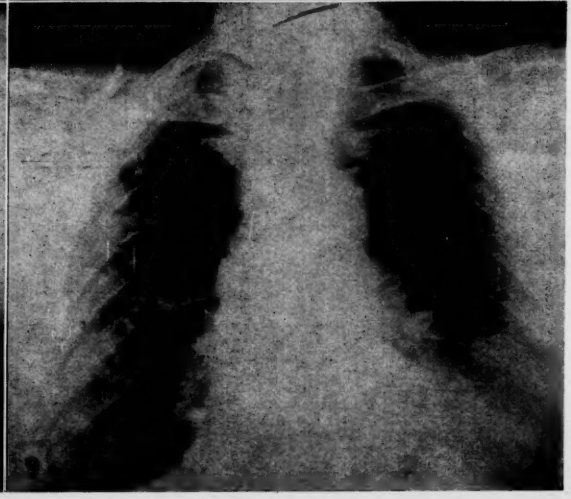
ILLUSTRATIONS TO THE ARTICLE BY W. M. MAXWELL AND P. E. CAMPBELL.



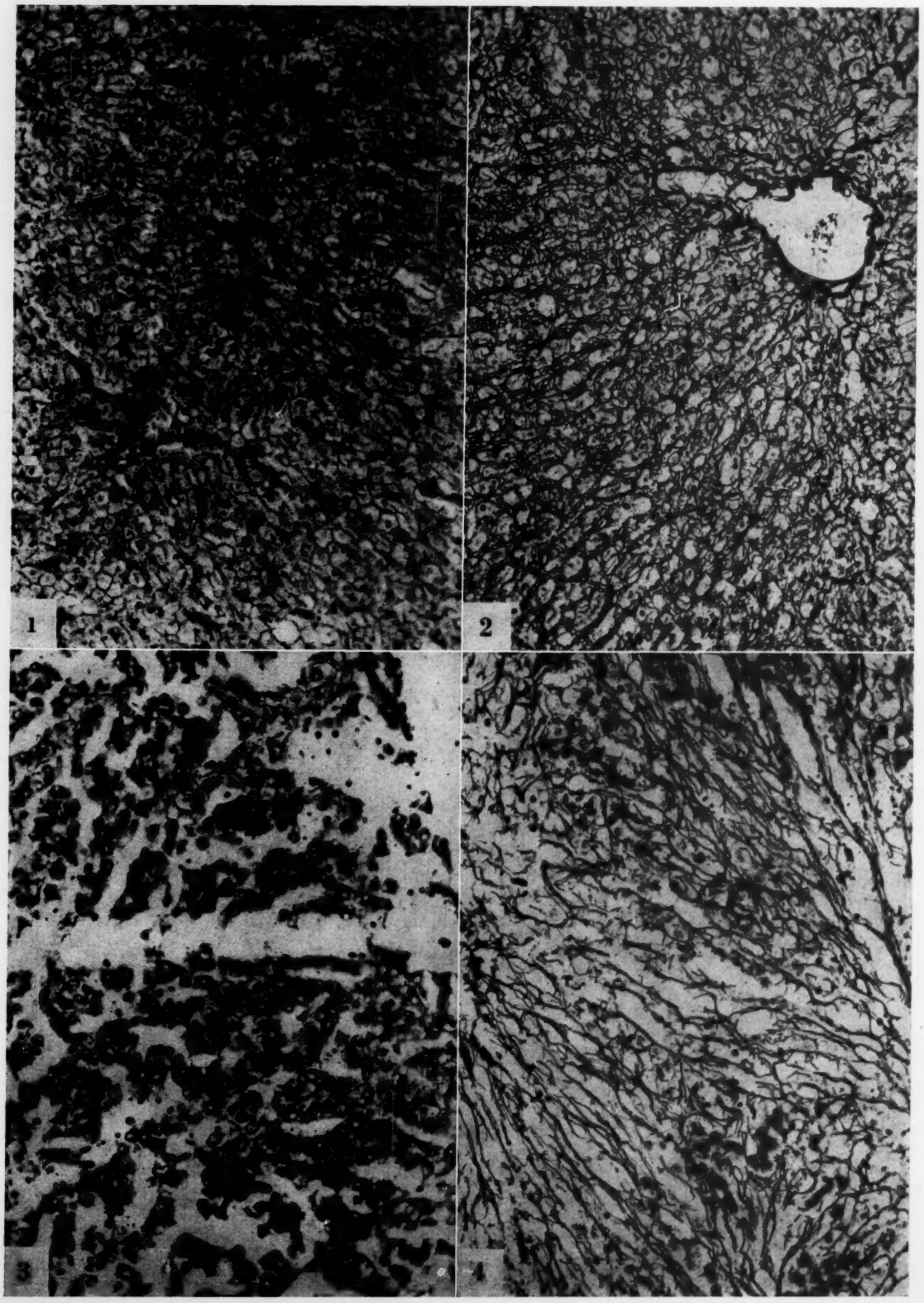




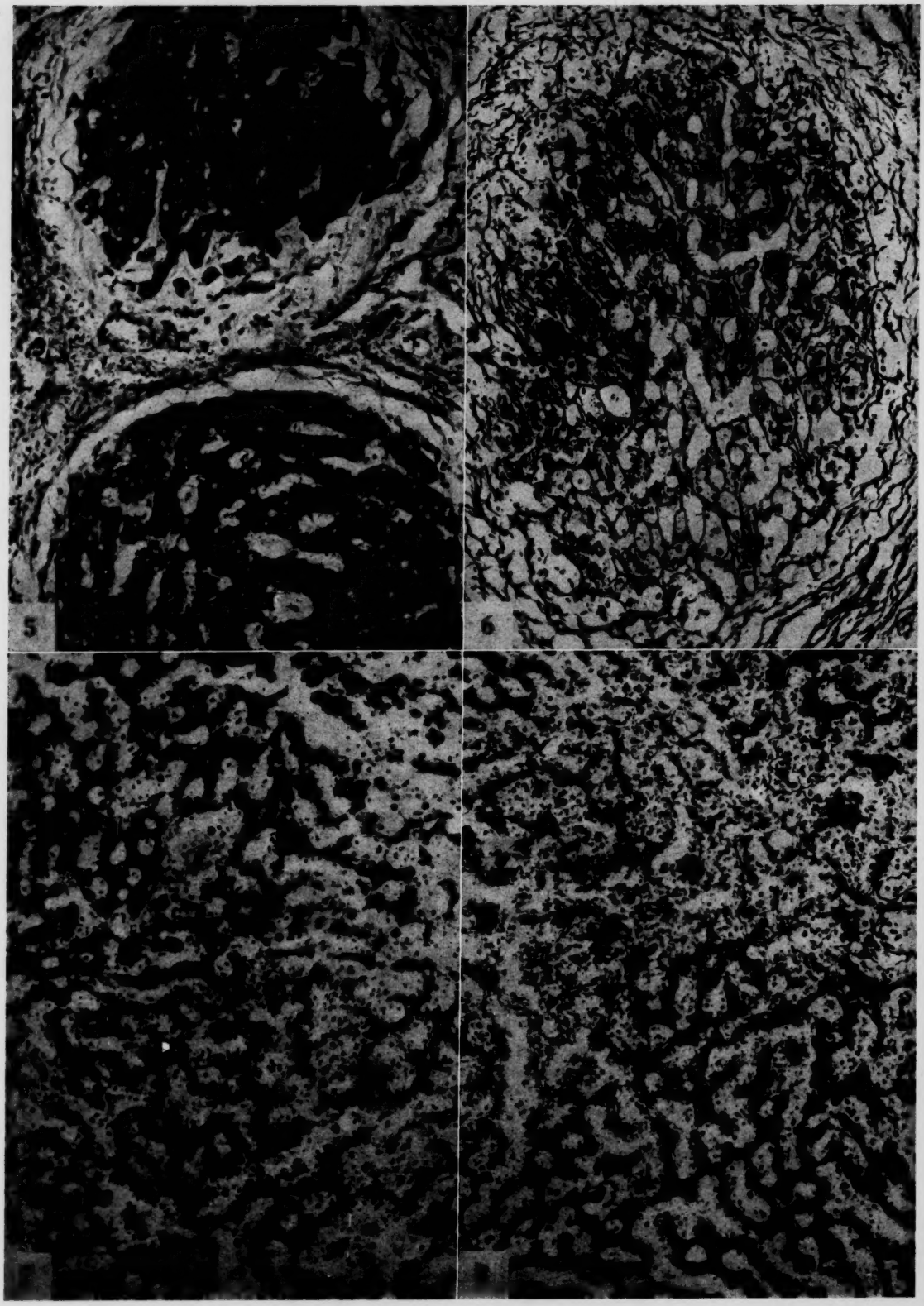




ILLUSTRATIONS TO THE ARTICLE BY E. B. JONES.



ILLUSTRATIONS TO THE ARTICLE BY E. B. JONES.



If a canalicular system is present, it is in cases of chronic venous congestion that it should be most easily demonstrated, especially if this system is composed of rigid tubes. Again, the disruption of this canalicular system should result in an intense jaundice. The truth is, however, that in uncomplicated chronic venous congestion canaliculi are scanty, and jaundice, if present, is at most only slight. Plainly bilirubin excretion continues without serious impairment. The slight jaundice or icterus that sometimes occurs could well be attributed to lack of oxygenation of the parenchyma, a failure in function that is not confined to liver cells.

It can be said that whenever there is gross derangement of the canalicular system, the liver cells can still conjugate bilirubin, and the esterified bile can pass back into the circulation. In hepato-cellular damage, provided that sufficient liver cells can function, jaundice will not supervene; also, as the mass of liver tisue is ultimately reduced below the number of efficient liver cells necessary to esterify free bilirubin, jaundice appears.

Summary.

It appears that between the liver cells there are clefts or gutters. It is largely into these clefts that the products of cell metabolism may drain, and plasma seeping through these channels could transport these products to the blood-stream.

The canalicular collecting system, according to the classical theory, is stated to be composed of canals or tubules. It is difficult to imagine any such system not being continuous or not consisting of tubules, since if this was not so it would be necessary to visualize the secretion flowing against the positive-pressure gradient exerted by the blood-stream in the opposite direction.

Conclusion.

A method has been developed which, while inhibiting the silver impregnation of reticular structures of the liver, demonstrates the so-called bile canaliculi.

The results are not inconsistent with Andrews's hypothesis that bile is secreted from the blood-stream by the bile-duct epithelium and excreted into the bile ducts.

Acknowledgements.

I wish to record my appreciation of the support given me by Dr. C. J. M. Walters, General Medical Superintendent and Chief Executive Officer of the Prince Henry Hospital, and to Mr. Harold Fisher for his untiring efforts on my behalf. I wish to thank the Department of Illustrations, New Medical School, University of Sydney, for the photomicrographic preparations. To Dr. C. E. Percy and Dr. R. W. Sinclair of the N.S.W. Police Department I am grateful for the use of post-mortem material. To Dr. R. J. Bartholomew and Professor F. Magarey for their valuable advice and equally valuable criticism I am much indebted.

References.

AHRENS, E. H., JR., HARRIS, R. C., and MACMAHON, H. E. (1951), "Atresia of the Intra-Hepatic Bile Duct", *Pediatrics*, 8: 628.

ANDREWS, W. H. HORNER (1955), "Excretory Function of the Liver: A Re-assessment", *Lancet*, 2: 166.

CARLETON, H. M. (1946), in "Schafer's Essentials of Histology", 14th Edition: 227, 594.

MAXIMOW, A. A., and BLOOM, W. (1939), "A Text Book of Histology", 3rd Edition: 418.

Legends to Illustrations.[1]

FIGURE I.—Normal liver, stained for bile canaliculi.

FIGURE II.—Normal liver, stained for reticulum.

FIGURE III.—Liver, infectious hepatitis, stained for bile canaliculi.

FIGURE IV.—Liver, infectious hepatitis, stained for reticulum.

FIGURE V.—Liver, portal cirrhosis, stained for bile canaliculi.

FIGURE VI.—Liver, portal cirrhosis, stained for reticulum.

FIGURE VII.—Liver, chronic venous congestion, stained for bile canaliculi.

FIGURE VIII.—Liver, chronic venous congestion, stained for reticulum.

[1] Magnification in each case × 150.

Reports of Cases.

ATAXIA-TELANGIECTASIA.

By JOHN BEVERIDGE,

From the Institute of Child Health and the Royal Alexandra Hospital for Children, Sydney.

INTEREST has been aroused in a syndrome of ataxia, telangiectasia and sino-pulmonary infection by two reports from California, both of which appeared in April, 1958. In one of these (Boder and Sedgwick, 1958) seven cases were reported; one of the children died, and the autopsy findings were recorded; there is also a posthumous case history of an eighth child. The other (Centerwall and Miller, 1958) presented details of two children, one of whom died; and the autopsy findings in this case are recorded. These two reports include one case in common. Shy and Wells (1957) report the cases of two siblings who had "progressive familial choreo-athetosis with cutaneous telangiectasia", but no mention is made in their report of sino-pulmonary disease.

The essentials of the syndrome are as follows: (i) familial incidence; (ii) early development of choreo-athetoid movements; (iii) progressive ataxia of cerebellar type; (iv) recurrent bronchial disease, becoming chronic, with the eventual development of bronchiectasis; (v) recurrent nasal discharge and sinusitis, becoming chronic; (vi) symmetrical telangiectases, always on the conjunctivæ, usually on the ears, and often elsewhere. On the negative side, it is not usual for these children to be mentally retarded, although their lack of expression and difficulty with speech and coordination may give the superficial impression of mental retardation.

The clinical course of the neurological troubles is a variable one, but there is commonly slow and progressive deterioration to the stage of being bedridden. Attempts have been made, of course, to link this form of familial ataxia with other disorders of the central nervous system associated with vascular findings—for example, von-Hippel-Lindau's disease and the Sturge-Weber syndrome. Rendu-Osler-Weber disease (hereditary hæmorrhagic telangiectasia) is characterized by vascular lesions almost anywhere, especially on the mucous membranes, but also in the eye, brain and lung; ataxia, however, is not part of this syndrome. The symptom complex fits more into the broad group of heredo-familial ataxias. Of the ataxias, the von Hippel-Lindau's disease presents most similarities with progressive retinal and cerebral angiomata and progressive loss of vision and ataxia; but it is clear from the clinical and pathological findings that the two conditions are quite dissimilar.

The pathological findings are limited to two case reports, although pneumoencephalograms give evidence of cerebellar atrophy in other cases. The central nervous system was normal on macroscopic examination, but microscopic examination showed primary chronic progressive cerebellar degeneration involving the Purkinje cells, the granule cells and the basket cells. There was coincidental secondary shrinkage of the cerebellar white matter; there were also some minor changes in the dentate and olivary nuclei, also thought to be secondary. The small veins of the cerebellar leptomeninges, white matter and dentate nucleus were enlarged, thin-walled and engorged, as has been found in Rendu-Osler-Weber disease.

The naso-pulmonary troubles are not connected with the central nervous system disorder by way of muscular weakness or through the patient's being bedridden. Children who are active and ambulant develop such troubles, and there is no evidence of respiratory muscle weakness. The clinical and radiological findings have nothing to distinguish the condition from idiopathic sino-bronchitis and sino-bronchiectasis. The pathological findings at the two autopsies reported were of gross bronchiectasis with pulmonary fibrosis; there was no evidence of any pulmonary

vascular anomaly. The respiratory disease appears to be the most important prognostic factor for life, for of the three fatal cases reported, one was that of a girl, who died at the age of 11 years from respiratory infection, another that of a man, aged 25 years, who died from pneumonia complicating measles, and the third that of a boy, who died at the age of eight years from overwhelming chronic pneumonia despite long-term antibiotic therapy.

Case I.

John C., a male patient, was born on March 31, 1950. The family history is shown in Figure I. A maternal cousin suffers from "spasticity", but has no red eyes or other telangiectases. Inquiry into the patient's previous health showed that he had suffered from varicella, morbilli and pertussis. He had been immunized against diphtheria and poliomyelitis. He had been born normally after a normal pregnancy. The neonatal period was normal. It was realized very early, possibly at his birth, that he had red eyes. His mother never thought that his muscle tone was normal; his head control was poor, and when he was sitting (at the age of eight months) he frequently slumped forward. His wrist control was likewise weak, and his hands used to drop things.

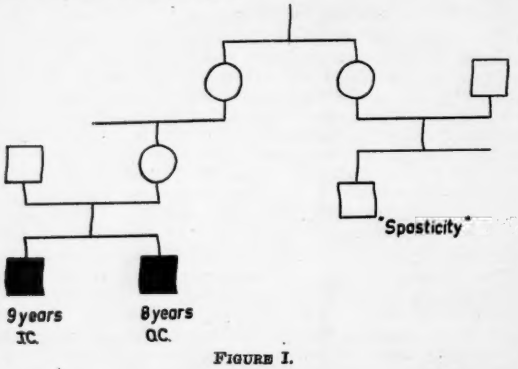


FIGURE I.

By the age of eighteen months he was walking; rather, "he ran before he could walk", in a clumsy fashion. At that time he had an attack of bronchitis—running nose, cough and fever. Thereafter, for the next four and a half years, he had about three such episodes per year. During all this time he had writhing movements of his upper limbs, his balance was generally poor but worse at times, and his mouth was constantly open and dribbling. At the age of about four years telangiectases were noted in the flexures of his elbows and knees.

In 1956, at the age of six years, he was referred to the writer suffering from pertussis. At that time he had a cough for three months, but subsequently had no more respiratory troubles until November, 1958. During this time, difficulty with balance, writhing movements and dribbling persisted. Speech became fairly clear, he learnt to dress himself and attended school, where he was not much behind the average for his age.

In November, 1958, he had a severe respiratory illness with nasal discharge, cough, fever and toxæmia, and was admitted to another hospital. He improved well on treatment, but had a relapse six weeks later. Since then he has continued to have a loose cough and has been receiving continuous treatment with chloramphenicol; his care at present is undertaken by a local medical practitioner, the parents having moved from the area of the practitioner who originally referred him. It is reported that if chloramphenicol therapy is at any time suspended, fever and toxæmia soon reappear.

Since November, 1958, his difficulty with balance has increased.

On physical examination, the patient was seen to be of average build, with a vacant expression and open dribbling mouth (Figures II and III, child on right). He appeared to have some difficulty in fixing his gaze. Smiling was readily elicited, but the smile was slow to develop. The skin of the forehead, of the bridge of nose and over the cheek bones was thin, pale and atrophic. There were telangiectases on the bulbar and palpebral conjunctivæ (Figure IV[1]), on the ears, on the root of the neck, and on the flexures of elbows and knees. There was moderate clubbing of the fingers. He had difficulty in fixing his gaze, and a wandering type of nystagmus, not truly lateral, was present. There was mild ptosis, but the lids could be retracted voluntarily. The optic fundi were normal. Other cranial nerve functions seemed intact. He stood on a wide

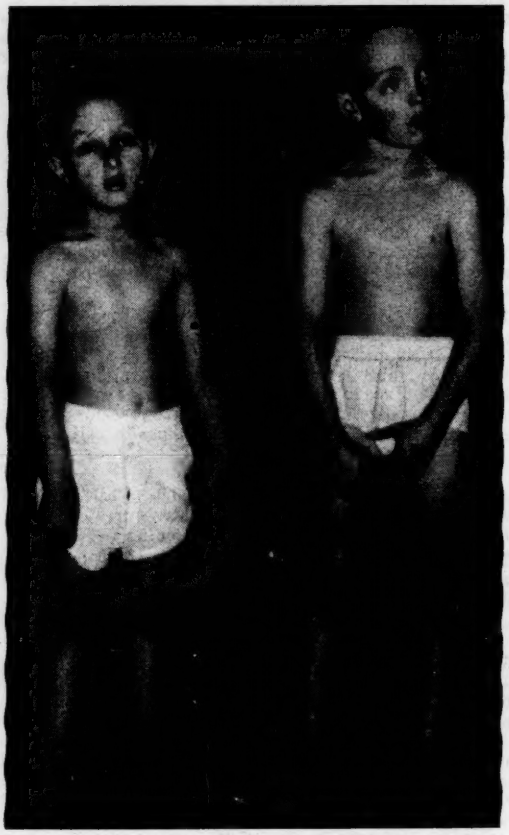


FIGURE II.

base, unsteadily, and there were writhing movements of his upper limbs; balance was a little worse with his eyes closed. He walked unsteadily and frequently stumbled. There was generalized hypotonia of limb muscles, and it was not possible to elicit the deep reflexes in the lower limbs. Muscle power was fair. The superficial reflexes were normal. Tests of coordination gave surprisingly normal results. All modalities of sensation appeared normal. Hearing was moderately impaired, though the ear drums appeared normal. There was no detectable abnormality of his nose or fauces at this examination. He had a loose cough, and medium râles were audible over all the areas of the chest. The heart and abdomen were normal on clinical examination.

A number of investigations was undertaken. On September 30, 1958, an X-ray examination of the paranasal sinuses showed that most of the ethmoid cells and the antral sinuses were opaque, the result of the gross mucosal swelling and/or fluid. An X-ray examination of the chest showed appearances within normal limits.

[1] For Figures IV, V and VII see art-paper supplement.

Case II.

Owen C., a male patient, was born on August 24, 1951. The family history is shown in Figure I. He had suffered from varicella, morbilli and pertussis, and had been immunized against diphtheria and poliomyelitis. The pregnancy had been normal, and a normal delivery had followed surgical induction of labour. The neonatal period was normal. In spite of a series of respiratory infections, his mother thought that Owen "felt" more normal than John; his muscle tone was much better. He had bronchopneumonia at the age of three weeks, at which time John also had his first respiratory illness and thereafter the brothers had respiratory infections at the same time, about three times a year until 1956, when both had pertussis.

FIGURE III.

After this Owen was likewise free of respiratory trouble until November, 1958. Although his muscle tone was better than John's, he was noticed to lean to one side when he started to walk, at the age of 18 months, and he had some difficulty in maintaining his balance. Some involuntary writhing movements were noted at that age, and his mother remarked on the "clawing" of his toes. His mouth was open, and he dribbled incessantly. His reddened eyes were not apparent until the age of four years, and near that time scaling areas of skin were noted on his neck and arms. His speech has never become as distinct as his brother's, and at the time of writing he has severe dysalia. His mother thinks he is of average intelligence compared with his school fellows. In November, 1958, he had bronchopneumonia at the same time as John. He still has a little cough, but no longer needs the continuous chemotherapy which John is receiving.

On physical examination, he was seen to be of average build for his age, and his vacant expression and open dribbling mouth were very similar to his brother's (Figures II and III, child on left). A slow smile was readily produced. The skin on the forehead, the bridge of the nose and the cheeks was thin and atrophic, and there were pale scaling areas on the neck, back and arms (Figure V). There were telangiectases on the palpebral and bulbar conjunctiva and on the ears. Clubbing of the thumbs of moderate degree was present. Poverty of facial expression and slight lateral nystagmus were noted. Both optic disks were pale, but not definitely atrophic. The speech was extremely difficult to comprehend. Hearing and the function of other cranial nerves seemed normal. There were crusts of dried secretion in his nose, and medium râles were scattered diffusely throughout his chest. The ear drums were opaque, reddened and retracted. He stood unsteadily on a wide base (Figure II), making writhing movements of the upper limbs; the unsteadiness was not increased by closing his eyes. He walked fairly steadily and without stumbling and falling. Coordination tests were performed surprisingly well. Limb tone was moderately reduced, and the deep reflexes were difficult to elicit. The superficial reflexes were normal. All modalities of sensation seemed normal.

In February, 1956, when the boy was in the Royal Alexandra Hospital for Children with pertussis, the following investigations were performed. An X-ray examination of his chest revealed no abnormality. A blood count gave the following information: the hæmoglobin value was 8·5 grammes per 100 ml.; the leucocytes numbered 7500 per cubic millimetre, 6000 being neutrophils, 900 (12%) lymphocytes and 225 (3%) monocytes. The cerebro-spinal fluid was normal. The erythrocyte sedimentation rate (Westergren) was 14 mm. in one hour. X-ray examination of the skull and long bones revealed no abnormality. Microscopic examination of the urine revealed no abnormality. An electroencephalogram was normal. Aspiration biopsy of bone marrow revealed some increased normoblastic activity and red-cell maturation. Further X-ray studies were undertaken on September 30, 1958, with the following findings. Both antra were completely opaque, owing to the presence of mucosal swelling and/or fluid. Some generalized enlargement of the heart was present, but the lung fields were within normal limits.

Case III.

J.S., a male patient, was born on May 5, 1947. The family history is shown in Figure VI. He had suffered from pneumonia twice, at the age of four years, had undergone an appendicectomy at six years, had had varicella at seven years and mumps at eight years, and had had his tonsils and adenoids removed at eight years. He had been immunized against diphtheria, pertussis and poliomyelitis. There had been no abnormality connected with the pregnancy, confinement or neonatal period. He had sat up at seven months, crawled at nine months, walked around his playpen at 12 months and talked at 12 months. He had first been admitted to hospital on September 28, 1949, in the care of Professor Lorimer Dods. He was then aged two years and four months, with the history that ever since he had begun to walk he had been unsteady, but shortly before his admission to hospital the unsteadiness had become worse. He had had some dysphagia for nine months and some difficulty in the use of his arm for several months. Examination of the child revealed no obvious abnormality apart from his walking with his legs wide apart and some unsteadiness on walking. The cerebro-spinal fluid was normal, and the blood gave negative responses to the Wassermann and Kline tests. An X-ray examination of the skull revealed no abnormality. The boy was admitted to hospital for the second time on January 17, 1959, at the age of 11 years and 9 months, and remained until March 1. He had a fall when attempting to walk at the age of 12 months, and after this was unwell for a few weeks. At the age of 18 months he was walking very well.

At the age of two years it was first noted that he had difficulty in balance and was a little unsteady on walking. He was able to commence school at five years, and at that time was given an intelligence test, the result of which was said to be normal. However, his difficulty with

walking progressed to such an extent that he could not attend school after the age of six years. When he was aged seven he found it impossible to stand or walk without assistance. At the age of 10 years he began to have difficulty in feeding himself; an intention-type tremor developed at that time. He could not, at the second admission to hospital, feed himself or drink from a cup. He could ride a tricycle if placed in position on it. Mentally, he was considered by his parents to be as bright and alert as his siblings.

He had suffered for years from recurrent upper respiratory tract infections, and he had acute coryza at the time of his admission to hospital. For some years he had had a daily loose cough, but it was difficult for him to produce sputum. He was thin and rather pale. His face showed poverty of expression, but his eyes betrayed his anxiety in his new surroundings. He never smiled, but at times was moved to tears. The superficial impression gained was that he was mentally retarded, but this was dispelled by his behaviour under observation. There was some clubbing of his fingers.

The most outstanding feature of the examination of the central nervous system was the gross difficulty in coordination in all motor functions, with disturbed speech and gross intention tremor. Motor power was generally poor. The tone of the skeletal muscles was fairly good, although a cogwheel sensation was perceptible at the extreme range of extension of the knees. Sensation was apparently normal, and the function of the cranial nerves, apart from the immobile facial expression, was normal. The optic fundi appeared normal. There was some congestion of the nasal mucosa, but the chest was normal on clinical examination.

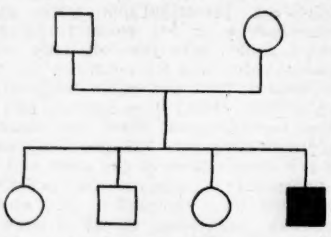


Figure VI.

The findings which were diagnostic of ataxia-telangiectasia were the telangiectases present on the conjunctivæ, the ears (Figure VII) and the side of the neck. These vascular phenomena were symmetrical and bright red in colour. An associated finding was the presence of atrophic skin on the nose and skin in the bat's-wing distribution. Investigations performed at this time gave the following results. No abnormality was detected in the skull on radiological examination. An X-ray examination of the chest revealed slightly increased broncho-vascular markings in the lingula and the lower lobe of the left lung. An X-ray examination of the paranasal sinuses revealed opacity of both antra. The Mantoux test (1/1000) produced a negative result. Microscopic examination of the urine revealed no abnormality. The electroencephalogram was normal.

Discussion.

These three children illustrate all the features of this condition. The two brothers demonstrate clearly the hereditary nature of the disorder; Dr. R. Gillott was kind enough to examine all the available relatives of J.S., and could find no evidence of any similar disorder.

The telangiectases are the diagnostic feature, of course, but, as in Owen's case, may not be present at an early age. All three of these children were regarded as having conjunctivitis at some time because of the "red eyes". The two brothers, John and Owen C., were suspected of measles; J.S. was at one time treated with zinc sulphate eye drops to help his "chronic conjunctivitis". The telangiectases are strictly symmetrical and extend progressively to the butterfly area of the face, neck, ears, hard and soft palates, dorsa of the hands and feet, and flexures of the elbows and popliteal region. Accompanying the telangiectases on the face in the three cases here reported is a considerable degree of skin atrophy; this does not seem to be reported by others. This atrophic state is present elsewhere in Owen C. (Figure V).

The facial expressions and postural attitudes, seen well in Figures I and II, are characteristic; mild choreo-athetoid movements were seen in all three. In addition, there is drooling of saliva. Fortunately, two children seem to have an equable disposition and ready sense of humour, which helps greatly in the adjustment to the affliction. These children illustrate, too, the way in which mental retardation is first suspected, but then discarded from consideration.

The ataxia appears of cerebellar type. The severity obviously varies from patient to patient, and the symptoms of incoordination become progressively more severe in each affected individual. Speech is characteristically slow, slurred and scanning, with poor breath control. Eyeball movements are abnormal, but dissection of the abnormalities is difficult. There may be an ordinary type of lateral nystagmus, or a difficulty of conjugate deviation and of convergence.

The frequent sino-pulmonary infections are typical. There the story is one of recurrences, leading to a chronic state of persistent nasal discharge and cough. Eventually bronchiectasis develops. These children as yet have no evidence of parenchymal lung disease on plain radiographic studies, and this makes bronchiectasis extremely unlikely. It was not considered justified to undertake bronchography to satisfy academic curiosity. Gamma-globulin studies have been undertaken by others (Centerwall and Miller, 1958) and the results have been found to be normal in one child and slightly low in another. These studies were not undertaken on these children.

Summary and Conclusion.

The histories are presented of three children who suffer from a condition whose features include recurrent, and then chronic, sinus and bronchial infections, telangiectases of skin and mucosæ, and central nervous system disorders including ataxia. These and other features, such as the familial incidence, are discussed, and reference is made to similar reports in other journals. The pathological findings in fatal cases, as described in these reports, are briefly recorded.

It is believed that the condition here described is a separate entity; although many cases have not yet been reported, it is probably not too uncommon, for the writer has knowledge of other patients at another institution (Reye, 1959). With wider knowledge of the many unmistakable features of the condition, more cases will be recognized.

References.

Bodek, E., and Sedgwick, R. P. (1958), "Ataxia-Telangiectasia", *Pediatrics*, 21: 526.

Centerwall, W. R., and Miller, M. M. (1958), "Ataxia, Telangiectasia and Sino-pulmonary Infections", *A.M.A. J. Dis. Child.*, 95: 385.

Reye, Corrie (1959), personal communication.

Wells, C. E., and Shy, G. M. (1957), "Progressive Familial Choreo-athetosis with Cutaneous Telangiectasia", *J. Neurol. Neurosurg. Psychiat.*, 20: 98.

HAMMAN–RICH SYNDROME (DIFFUSE INTERSTITIAL PULMONARY FIBROSIS).

By W. M. Maxwell, M.R.C.P., M.R.A.C.P.,

and

P. E. Campbell, M.B., B.S.,

Royal Melbourne Hospital, Melbourne.

Early in 1958, the diagnosis during life of a case of the Hamman-Rich syndrome led us to search for the frequency of this condition in the Melbourne hospitals. We find now that eight cases have been recognized in the last four years, and are thus prompted to bring this knowledge to wider notice.

In 1933, Hamman and Rich described three cases of pulmonary fibrosis which had progressed rapidly to death.

Specific changes were found in the lungs on pathological examination, the chief of these being the interstitial site of the fibrosis with thickening of the alveolar walls. By 1944 they had collected one further case which conformed to this clinical and pathological picture.

In the last fifteen years an increasing number of such cases has been reported. The only noteworthy alteration to the original description has been the emphasis on subacute and chronic forms, these actually proving to be much commoner than the acute type as in Hamman and Rich's cases. In addition, diagnosis during life has been facilitated by lung biopsy and lung function tests, and the therapeutic effect of cortisone has been assessed.

The condition can now be defined as a disease process of unknown cause, characterized pathologically by increasing and widespread interstitial pulmonary fibrosis of slow but occasionally rapid progress. The clinical features are progressive dyspnœa with cyanosis, clubbing of the digits and diffuse basal râles, whilst the pulmonary physiology indicates fibrosis and alveolar-capillary block. The findings on X-ray examination are those of widespread fibrosis, and on electrocardiography, variable right ventricular hypertrophy. The therapeutic measure likely to affect the disease is the administration of adrenal cortical steroid, which should be given early in the illness.

Our series confirms the impression given in the recent literature (Annotation, 1958) that this syndrome is not as rare as Hamman and Rich's original experience indicated. Large series reported are the 14 cases of Rubin and Lubliner (1957) and the seven cases of Forbes (1958); at the time of Rubin and Lubliner's paper, 63 cases had been reported in the literature.

Clinical Records.

We present the clinical and pathological findings of our first case in detail. Except for minor additional data, the findings in our other cases are given in the tables.

CASE I.—A male clerk, aged 51 years, was admitted to the Royal Melbourne Hospital on November 14, 1957, with a history of cough and dyspnœa present for two years. Dyspnœa had become severe recently, and was now associated with orthopnœa, restlessness and delirium at night. For three or four years he had noticed increased susceptibility to colds, and greater difficulty in shaking them off. Sixteen months previously he had had a severe attack of influenza which kept him in bed for seven weeks. His local physician noted finger clubbing, and requested a bronchoscopic examination, which showed no abnormality. When the patient returned to work, he was troubled by a dry cough. He had a further attack of influenza three months prior to his admission to hospital, this attack lasting two weeks. There was no history of exposure to dust at work, or of tuberculosis. His mother had been asthmatic for forty years.

On examination of the patient, he was seen to be a heavily built, plethoric man, dyspnœic at rest; the jugular venous pressure was raised 1 cm., and slight cyanosis was present. There was finger and toe clubbing, his temperature was 100·4° F., his blood pressure was 145/95 mm. of mercury, and his respirations numbered 24 per minute. The heart was not enlarged, but there was right ventricular over-activity with triple rhythm. Basal râles were present. X-ray examination of the chest revealed non-specific diffuse clouding and mottling throughout the lung fields, and bronchoscopic examination revealed reddening of the bronchial mucosa with scattered blobs of mucus. Lung function tests showed changes typical of fibrosis, and subsequent blood-gas studies indicated alveolar-capillary block typical of the Hamman-Rich syndrome. As a result of these findings, prednisolone therapy (10 mg. three times a day) was commenced and continued for one week, when the dose was decreased to 10 mg. twice a day. This led to some subjective improvement, and he was sent home for four weeks.

At the end of this time his condition had deteriorated and he was readmitted to hospital, where an electrocardiogram suggested cardiac infarction. Prednisolone therapy was discontinued, and digitalis and diuretics were given with benefit. ACTH, in a dosage of 20 units given subcutaneously, was substituted for prednisolone, and he again left hospital. However, the improvement was not maintained; he became weaker and more deeply cyanosed and was in constant respiratory distress, and he died shortly after his final admission to hospital on January 21, 1958, two years after the onset of the illness, and only two months after his first hospital admission.

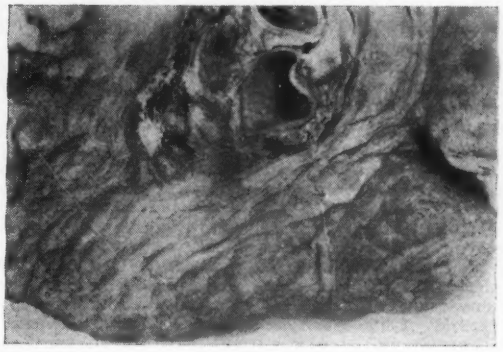


FIGURE I.
Case I: pleural surface, showing nodular appearance.

At autopsy the lungs showed coarsely nodular pleural surfaces (Figure I) that were free from adhesions. The underlying lung varied from a firm rubbery to a soft spongy consistency, and a few emphysematous bullæ were visible at the apices.

The cut lungs showed marked "honeycombing" (Figure II), and where this occurred the surrounding lung was firm and rubbery. The bulk of the lower lobes was solid, red and airless.

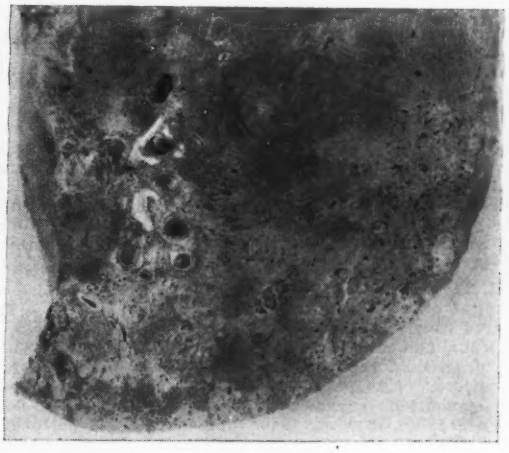


FIGURE II.
Case I: cut surface, showing honeycombing and fibrosis.

Microscopically, all blocks were abnormally congested. The main features were the dense fibrosis and the presence of an "epithelium" lining most of the alveoli and alveolar ducts. The fibrosis was gross, in places occurring as a sheet of mature fibrous tissue containing a few inflammatory cells, with only occasional spaces present within it. Elsewhere it was less extensive, and gave the impression of having arisen in an interstitial situation. Here it was often less mature in appearance, containing many fibroblasts and inflammatory cells, as well as dilated, congested capillaries. Large cysts were seen in this tissue, corres-

ponding with the macroscopic honeycomb appearance. They were more numerous in the peripheral parts of the lung.

The "epithelium" lining most of the alveoli and the majority of the cysts had the appearance of a syncytium, although in areas individual cells could be made out. These cells were large, 12-18μ in diameter, with prominent pink to purple cytoplasm and a large vesicular nucleus. They looked like macrophages, and many contained ingested blood pigment and other debris. Transitions from areas where these cells were separate to areas where they formed a syncytium were to be seen everywhere.

There were some ectatic bronchi present, and throughout the whole lung slight to moderate pulmonary arteriolar thickening, both intimal and medial, was evident.

Case II.—A barman, aged 56 years, was admitted to the Royal Melbourne Hospital in May, 1956, for investigation of extreme breathlessness developing after a cold four weeks previously. For five years he had noticed slight exertional dyspnœa. Treatment with cortisone was not really effective; but when it was stopped after the first three months' trial, it was quickly recommenced because of the consequent increased dyspnœa. By August, 1958, whilst still on maintenance doses of cortisone, he was dyspnœic on the slightest exertion, but there was no worsening of his condition.

No histological studies were available in this case, since lung biopsy was considered too hazardous.

Case III.—A female nursing aide at a tuberculosis sanatorium, aged 52 years, was first examined on April 10, 1958, at St. Vincent's Hospital. For twelve months she had been short of breath on exertion and at rest, requiring two pillows at night. She had an unproductive cough, and had lost one stone in weight. There was diffuse enlargement of the thyroid gland. As X-ray examination of the lungs showed diffuse pulmonary infiltration and tracheal deviation to the left, a provisional diagnosis of metastatic involvement of the lungs from carcinoma of the thyroid was made. ^{131}I studies revealed that the patient was euthyroid, and that there was no thyroid activity over the lung fields.

Lung biopsy was performed three months later. The chief pathological features were as follows: (i) A great increase in the thickness of the alveolar septa (Figure III).[1] The fibrous tissue composing these generally was mature, but parts were still vascular and obviously fibroblastic in nature. (ii) Cyst formation. (iii) Metaplasia of cells lining the alveoli and cysts. Present in some alveoli as a single layer of cells, in many areas they were banked up into a sheet of cells reminiscent of squamous epithelium. As in Case II, they appeared to be derived from macrophages. Vessels showed slight to moderate intimal thickening. The pleura was involved in the fibrotic process and was greatly thickened, but its surface was smooth.

Case IV.—A housewife and part-time shop assistant, aged 32 years, was admitted to the Royal Melbourne Hospital on September 5, 1956, with a history of a productive cough present for 12 months after an attack of influenza, and exertional dyspnœa for three months, which had progressed rapidly, so that she found difficulty with housework. An X-ray examination of the chest showed coarse, mottled, opaque areas throughout both lung fields (Figure IV). In May, 1958, lung biopsy was performed, and the biopsy specimen was reported as showing features of chronic bronchiectasis. In September, 1958, the lung biopsy specimen was reexamined, and the diagnosis of the Hamman-Rich syndrome was made. All the tissue was involved in a process of extreme alveolar septal thickening (Figure V). The fibrous tissue generally appeared œdematous and immature, but no fibrin was visible either in alveoli or in septa. Alveoli, where present, were lined by cuboidal cells and contained occasional clumps of macrophages. Large cysts were present throughout the specimen, lined by cuboidal to columnar epithelium and containing accumulated secretion. The majority had no suggestion of muscle or cartilage in their walls, which would point to an origin from bronchi.

[1] For Figures III, IV, V, VII, VIII and IX see art-paper supplement.

Case V.—A housewife, aged 56 years, was referred to the out-patient department of the Royal Melbourne Hospital in December, 1957, with a two years' history of marked shortness of breath on exertion. This had been accompanied by moderately severe hypertension and occasional angina, but treatment for this, including the administration of mecamylamine, had failed to relieve her dyspnœa. Her blood pressure was 190/110 mm. of mercury. Lung biopsy was considered, but was not carried out because of the patient's age and her history of myocardial ischæmia. Prednisolone therapy (10 mg. twice a day) has produced great subjective improvement, but the results of tests of pulmonary function have remained unchanged. Figure VI shows the clubbing of fingers in this case.

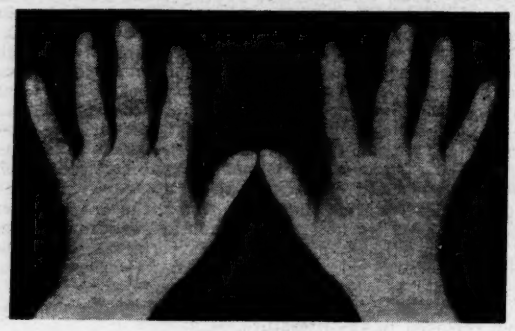


Figure VI.
Case V: clubbing of fingers.

Case VI.—A female pensioner, aged 60 years, was admitted as an in-patient to the Royal Melbourne Hospital in December, 1957, with a history of marked dyspnœa for five months. For the previous eight years she had noticed slight dyspnœa only, and this was considered due to her hypertension. (From the age of 12 to 14 years she had been treated at the Royal Children's Hospital for a "spot on the lung"; and when she left school she worked for a time in a corset factory, where she was exposed to a dusty atmosphere containing aluminium filings and teased horsehair.) The balance of evidence pointed to a diagnosis of the Hamman-Rich syndrome, and she was given prednisolone in a dosage of 40 mg. per day for three weeks. However, her condition deteriorated steadily till her death in March, 1958.

On pathological examination, the pleural surfaces of the lungs were smooth and slightly nodular. The cut surfaces showed marked consolidation and considerable honeycombing at the edges.

Microscopically, septal thickening was a prominent feature, and the septa were composed largely of mature fibrous tissue. Alveoli were much larger and fewer in number than in a normal lung, and most were lined by a single or double layer of macrophages giving the appearance of an epithelium. Scattered through some parts of the lung were small calcified areas ("conchoidal bodies") about 100μ in diameter, consisting of laminated plates of calcified material and surrounded by a zone of fibrous tissue (Figure VII).

The pulmonary arterioles showed slight medial and intimal thickening. Bronchiectasis was present in the lower lobe of the right lung. It was not extensive.

Case VII.—A male clerk, aged 50 years, was first admitted to the Royal Melbourne Hospital in February, 1952, with a history of persistent cough for two or three months following influenza. He had had exertional dyspnœa for 18 months and chronic sinusitis for many years. Respiratory distress progressed rapidly, and he died in November, 1952. A ten-day course of corticotrophin was not beneficial.

The pathological findings were similar to those in Case I. Especially noticeable were large cysts, lined by a layer of cells of identical appearance with those described in other

TABLE I.
Clinical Features and Response to Treatment.

Case Number.	Sex.	Age. (Years.)	Duration of Symptoms to February, 1959, or Death.	Cyanosis.	Clubbing.	Diffuse Râles.	Response to Steroid Therapy.	Initial Diagnosis.
I	M.	51	2 years.	+	+	+	Fair, unsustained.	Hamman-Rich syndrome.
II	M.	56	3 years.	+	++	+	Fair.	Sarcoidosis.
III	F.	52	2 years.	−	+	+	Fair.	Carcinoma of thyroid with pulmonary metastases.
IV	F.	32	3½ years.	−	+	+	Poor.	Sarcoidosis.
V	F.	56	3½ years.	+	+	+	Delayed—very good.	Hypertensive heart failure with pulmonary congestion.
VI	F.	60	9 months.	+	++	+	Poor.	Hamman-Rich syndrome.
VII	M.	50	11 months.	−	+	+	Poor.	Sarcoidosis, or virus pneumonia.
VIII	F.	37	1 year.	+	++	+	Very good.	Bronchopneumonia.
IX	M.	58	5 years.	+	+	+	Poor.	Hamman-Rich syndrome.

cases. Fibrosis was extensive and interstitial, and the fibrotic areas were generally œdematous, vascular and infiltrated with numbers of chronic inflammatory cells. Vascular thickening was prominent.

CASE VIII.—A housewife, aged 37 years, was first admitted to Fairfield Hospital in February, 1958, when she gave a history of approximately two months' shortness of breath, mainly on exertion, associated with non-productive cough. The dyspnœa was severe, relieved only by lying down. There was no history of an acute febrile episode or of purulent sputum. Lung biopsy was carried out on this patient, and the reader is referred to the article by Bennett (1959) for further details.

CASE IX.—A farmer, aged 58 years, was first examined in 1954, when he complained of troublesome dyspnœa following a recent attack of bronchitis. Cough and sporadic dyspnœa had commenced six years previously, but these symptoms were overshadowed by dyspepsia, which was found due to hiatus hernia. Lung biopsy was not carried out in this case because of the patient's poor physical condition. (See Figures VIII and IX.)

Discussion.

It has in the past year or two become widely recognized that the rate of progress of the lung fibrosis in this condition varies greatly, and this is illustrated by the rapid onset of symptoms in Case VIII and their slow development in Case IX. It is indeed striking that, in the eleven-year period 1933-1944, during which time Hamman and Rich could add only one further case to their three acute cases noted in 1933, they did not encounter even one patient with the more slowly developing syndrome which now seems to be the rule.

The patient who has this syndrome is usually middle-aged, the sexes being approximately equally affected. Although the disease may occur in childhood (Baar *et alii*, 1957), we have not encountered such a case. Symptoms often date from an upper respiratory tract infection.

Diagnosis.

The diagnosis can be strongly suspected on clinical grounds by relentless progression of dyspnœa in patients who have no heart disease, and who exhibit cyanosis, clubbing of the fingers and toes and diffuse râles. Emphysema, a frequent cause of dyspnœa, is a diagnostic possibility when these patients are examined initially, but it is excluded by the absence of the above-mentioned clinical features, and by the X-ray picture, which shows clear (or abnormally clear) lung fields.

Radiologically, the plain film of the chest shows the widespread streaky opacities of fibrosis with no specific localization in the lung fields; hence the only causes of pulmonary fibrosis that can be excluded on radiological grounds are those with characteristic upper zone distribution—namely, tuberculosis and possibly silicosis. In some of the Hamman-Rich cases honeycombing is present; this radiological-pathological term was coined by Oswald and Parkinson (1949) to describe cystic spaces in the lungs of diameter not greater than 1 cm. The pathological associations of honeycombing are varied, and Forbes (1958) is the first to have stressed its occurrence in the Hamman-Rich syndrome. Bronchographic studies in our cases have been too incomplete to allow of detailed reporting.

The electrocardiogram typically shows right ventricular hypertrophy. The findings in our cases are detailed in Table II.

Lung function tests are of great importance in assisting diagnosis. The initial step is the demonstration of the "restrictive" ventilatory defect of fibrosis, the characteristics of which are a small vital capacity with well-preserved maximum breathing capacity (M.B.C.) and moderate reduction of forced expiratory volume at 1 sec. expressed as a percentage of the vital capacity (F.E.V. 1·0/V.C. × 100; or F.E.V.% : normal, 75%). (In emphysema the vital capacity, while usually reduced, may be normal, but the M.B.C. is uniformly much reduced, as is the F.E.V. percentage also.)

That the fibrosis is interstitial in type is indicated by alveolar-capillary block; arterial blood-gas studies show that the carbon dioxide level after exercise remains normal, whilst there is a very marked increase in arterial anoxæmia. This is due to the greater diffusing power of carbon dioxide as compared with oxygen. In emphysema, on the other hand, progressive hypercapnia accompanies increasing anoxæmia.

Lung biopsy is diagnostic. It is essential and perfectly safe in the early case (Case VIII of this series; Pinney *et alii*, 1956); but in the advanced case, since the patient is unlikely to benefit with reference either to diagnosis or to subsequent therapy, the risks of thoracotomy with persisting collapse of the lung after operation exclude it as a routine procedure.

In differential diagnosis the common causes of widespread pulmonary fibrosis must be excluded. In Cases II, IV and VII sarcoidosis was suspected, but the absence of eye signs and skin lesions, the normal serum protein and serum calcium levels, the positive Mantoux reaction and the negative histological findings on liver biopsy (Case II) and lymph-node biopsy (Case IV) excluded this diagnosis in the individual cases.

Case III was believed initially to be one of secondary carcinoma of the lungs from a primary lesion in the thyroid; but lung biopsy finally excluded this possibility. Secondary carcinoma from primary growths in other sites,

TABLE II.
Laboratory Investigations.

Case Number.	Hæmoglobin Value. (Grammes per 100 Ml.)	Leucocytes per Cubic Millimetre.	Erythrocyte Sedimentation Rate. (Millimetres in One Hour.)	Bacteriological Findings in Sputum or Gastric Contents.	Response to Mantoux Test (1 : 1000).	X-Ray Examination of Chest.		Electrocardiographic Findings.	
						Fibrosis.	Honeycombing.	Right Ventricular Hypertrophy and *P. Pulmonale*.	Other.
I	16·7	13,000	67	No tubercle bacilli in sputum.	+	+			Non-specific.
II	17·3 (Later 21·8)	7000 (Later 6000)		No growth on attempted culture of sputum.		+	+		Normal.
III	15·9	10,700		No growth on attempted culture of sputum.		+			
IV	14·3	8000	29	No tubercle bacilli in gastric contents.	+	+		+	
V	13·3					+			Left ventricular hypertrophy.
VI	14·8	11,000	36		−	+			Ischæmic.
VII	17·0	6000		*Staphylococcus aureus*, coagulase-positive in sputum; no tubercle bacilli.	+	+			Normal.
VIII	12·9	12,000	2	*Streptococcus viridans* and pneumococci in sputum.		+			Normal.
IX	17·0					+	+		

such as breast, bronchus and stomach, can be excluded by clinical examination and barium meal studies.

The patient in Case V was for long regarded as suffering from hypertensive cardiac failure with congestion. In the early stages of the Hammon-Rich syndrome the fibrosis may be predominantly basal, and the clinical and radiological differentiation from pulmonary congestion may be difficult (Silverman and Talbot, 1953).

The patient in Case VI had, as an adolescent, been exposed to a dusty atmosphere containing aluminium. (In none of the other cases was there a history of possible pneumoconiosis.) The lungs were analysed *post mortem* for aluminium, but none was found. This patient presented some clinical signs of hyperthyroidism (which led to treatment with antithyroid drugs). These features have been noted by others (Silverman and Talbot, 1953), and are attributed to the high cardiac output.

Case VII was believed clinically and from lung biopsy to be one of chronic unresolved pneumonia. This condition is considered more fully in the pathological discussion, but it provides the most difficult problem in differential diagnosis, since many of the patients date the onset of symptoms from a febrile respiratory illness. However, the usual unilaterality of pneumonia offers the most important clue to the differentiation.

In differentiation from the collagen diseases, polyarteritis nodosa is excluded if there is no eosinophilia (Rose and Spencer, 1957). Scleroderma presents characteristic involvement of the œsophagus, even if skin lesions are absent. Lung changes in rheumatoid arthritis are

TABLE III.
Results of Lung Function Studies[1]

Case Number.	Vital Capacity in Millilitres: Predicted Normal in Parentheses.	Maximum Breathing Capacity: Predicted Normal in Parentheses. (L./min.)	F.E.V. (Normal, 70%).	Arterial Blood Gas Studies.			
				Oxygen Saturation.		Carbon Dioxide Content. (Volumes per Centum.)	
				Before Exercise (Normal, 97%).	After Exercise.	Before Exercise (Normal, 50-60).	After Exercise.
I	1380	76·8 (90±15)	85%	71%	49%	58	52
II	3310	78·9 (90±15)	24%	90%	79%	49	46
III	930 (3280)	43·8 (75±15)	96%	90%	74%	54	58
IV	1090 (3200)	73·3 (95±10)	74%	80%	61%	47	50
V	700 (2800)	58·4 (75±15)	100%	80%	55%	59	57
VI	—	—	—	—	—	—	—
VII	—	—	—	—	—	—	—
VIII	1156	38·2 (95±10)	—	—	—	—	—
IX	1670 (5000)	72·8 (90±15)	100%	85%	70%	51	41

[1] Normal figures from Baldwin *et alii* (1948)

TABLE IV.
Pathological Findings.[1]

Case Number.	Pleural Surface.	Extent of Lung Involvement.	Honeycombing.	Fibrosis.		Alveolar Septal Cell Proliferation.	"Conchoidal" Bodies.	Arteriolar Thickening.	Bronchiectasis.
				Early.	Late.				
I	Nodular, smooth, not thickened.	Entire lung.	++	+	+++	++++	–	+	+
II	——		+ (X rays)		–	–	–	–	–
III[2]	Nodular, smooth, thickened.	Entire lung.	+	+	+++	++	–	+	–
IV[2]	Thickened, a few adhesions.	Entire lung.	+	++	+	+++	–	–	–
V		—	–		–	–	–	–	+
VI	Smooth, nodular.	Entire lung.	+		+++	++	+	+	–
VII[2]	Smooth, a few old adhesions.	Entire lung.	++		+++	+	–	++	–

[1] Cases VIII and IX are omitted, as no information was available.
[2] Biopsy specimen examined.

fully discussed by Forbes (1958). The bronchiectasis patient presents finger clubbing and fibrosis; but the dilated bronchi are usually demonstrated early in the course of the disease.

Ætiology.

The ætiology is still unknown, infection, hypersensitivity and collagen disease theories having been considered (Rubin and Lubliner, 1957). We believe that the condition may well be the sequel of the action of a number of ætiological agents, each producing inflammatory œdema of the alveolar walls, so that organization occurs, rather than resolution. How the change is brought about, and why it is confined largely to the alveolar septa, seems to be the crux of the problem requiring elucidation. Recent work suggests that an auto-immune mechanism may be responsible (Reid, 1958).

Another interesting paper is one by Andrews (1957), in which he describes pulmonary fibrosis (of a type similar in many ways to that of the Hamman-Rich syndrome) caused by long-standing obstruction to the pulmonary veins.

Pathological Features.

The chief pathological features in the various cases are listed in Table IV.

The nodular, scarred, but smooth pleural surface, the firm, rubbery lung, honeycombed with cysts, the widespread fibrosis of an interstitial distribution and the constant presence of alveolar septal cell metaplasia were well exemplified in all the cases described.

Hamman and Rich described four stages of the histopathological changes. We thought that for the purposes of classification this tended to be artificial, as one could see all four stages of development in different parts of the lung in many cases. Estimate was therefore made of the age of the fibrous tissue, and the fibrosis was classified as early or late (mature). On this basis, the majority of cases showed late changes.

In our opinion one of the most striking features is the appearance of the cells which line the alveoli. Their presence in the cases discussed and in others described has been such a constant feature that they can probably be regarded as a useful aid to diagnosis. However, such proliferation, or metaplasia, may occur in the alveoli in association with several chronic lung conditions—for example, sarcoidosis, lung abscess, bronchiectasis and beryllium pneumonoconiosis, to name a few—and it is only when it is associated with the characteristic septal thickening of the Hamman-Rich syndrome that it is of value as a diagnostic feature.

The next most striking feature is the extensive fibrosis, and no part escapes some septal thickening or scarring. Where the fibrosis is extensive, several consecutive fields may be examined before a space is found, lined in most cases by the typical epithelium described above. The conchoidal bodies described by Forbes (1958) were seen in one case. They closely resemble the concretions present in lungs in the condition called microlithiasis alveolaris pulmonum, first described by Puhr in 1933. They probably represent calcified necrotic debris derived from the desquamated cells lining the alveoli.

Differentiation from other conditions is usually made *ante mortem* (*vide supra*), but the most difficult histological differentiation is from unresolved pneumonia. Here, however, the whole lung is almost never involved, the fibrosis in chronic pneumonia being the result of the organization of intraalveolar exudate, whereas in the Hamman-Rich syndrome fibrosis is initially, at any rate, in the alveolar septa, and is widespread, involving almost the whole lung to a greater or lesser degree. Lung involvement in sarcoidosis is characteristically nodular, typical tubercle-like structures can be found in various stages of development scattered through the lung parenchyma, and the old inactive lesions are represented by focal scars surrounded by emphysematous but otherwise normal alveoli in which no suggestion of septal thickening is present.

Treatment.

The only effective treatment for this condition is adrenal cortical steroid. The patients who respond are those in whom the condition is diagnosed early, whilst in the acute phase, and when the fibrous tissue is immature. (Case VIII; Gleishman *et alii*, 1958; Freedman *et alii*, 1958; Harris *et alii*, 1957; Hoff, 1958; Pinney *et alii*, 1956; Van Slyk, 1957.) Case V is unusual, both in showing a satisfactory response to steroid therapy when the fibrosis was already chronic, and in the latent period of several months before improvement was noted. Cortisone and its analogues may actually be dangerous for the patient, should the therapy be stopped for any reason, for several authors record cases of abrupt and fatal deterioration in their patients' condition in such circumstances (Peabody *et alii*, 1953).

Summary.

Nine cases of the Hamman-Rich syndrome are reported, eight of them having occurred in the last four years.

The clinical features of these cases conform to the now well-defined pattern of a chronic disabling and usually fatal illness. The rarity of acute progress of the condition is further emphasized.

The clinical and pathological differential diagnosis is considered in detail, unresolved pneumonia providing the greatest difficulty in this respect.

The contributions of lung function tests and lung biopsy are discussed.

Pathologically, in all cases in this series extensive septal cell metaplasia was present in addition to interstitial fibrosis.

The only effective treatment is the administration of cortisone and its derivatives, which must usually be given early in the disease to be successful, as is shown in one of the cases. Early diagnosis is therefore a vital responsibility of the attending physician.

Acknowledgements.

We are grateful to Dr. G. A. Penington, Dr. W. McI. Rose, Dr. Luke Murphy, Dr. A. J. Goble, Dr. J. H. Bolton, Dr. H. McLorinan and Dr. W. E. King for permission to report cases under their care. Dr. Goble and Dr. Bryan Gandevia have assisted with the pulmonary function studies and have given much helpful advice. The illustrations have been prepared by Mr. Roy Inglis, of the Royal Melbourne Hospital, and by Mr. J. Murphy and Miss Omond, of the Royal Children's Hospital.

References.

ANDREWS, J. C., JR. (1957), "Five Cases of an Undescribed Form of Pulmonary Interstitial Fibrosis Caused by Obstruction of the Pulmonary Veins", *Bull. Johns Hopk. Hosp.*, 100: 28.

ANNOTATION (1958), "The Hamman-Rich Syndrome", *Lancet*, 1: 730.

BAAR, H. S., and BRAID, F. (1957), "Diffuse Progressive Interstitial Fibrosis of the Lungs in Childhood", *Arch. Dis. Childh.*, 32: 199.

BALDWIN, E. DE F., COURNAND, A., and RICHARDS, D. W., JR. (1948), "Pulmonary Insufficiency: Physiological Classification, Clinical Methods of Analysis, Standard Values in Normal Subjects", *Medicine*, 27: 243.

BENNETT, N. McK. (1959), "Diffuse Interstitial Fibrosis of the Lungs (Hamman-Rich Syndrome) Successfully Controlled by Prednisolone", MED. J. AUST., 2: 84.

FLEISHMAN, S. J., BOSMAN, A. R., and FULLER, D. N. (1958), "Diffuse Interstitial Fibrosis of the Lungs. Successful Treatment of a Case with Adrenal Steroids", *Amer. J. Med.*, 24: 823.

FORBES, I. J. (1958), "Diffuse Interstitial Pulmonary Fibrosis and Honeycomb Lung", *Aust. Ann. Med.*, 7: 205.

FREEDMAN, A., and DEATON, W. R. (1958), "Diffuse Interstitial Fibrosis of the Lungs (Hamman-Rich Syndrome). Successful Palliation of a Case with Steroid Therapy", *Dis. Chest.*, 34: 557.

GRANT, I. W. B., HILLIS, B. R., and DAVIDSON, J. (1956), "Diffuse Interstitial Fibrosis of the Lungs (Hamman-Rich Syndrome). A Review with a Report of Three Additional Cases", *Amer. Rev. Tuberc.*, 74: 485.

HAMMAN, L., and RICH, A. R. (1933), Clinical Pathologic Conference, *Int. Clin.* 43, 1: 197.

HAMMAN, L., and RICH, A. R. (1944), "Acute Diffuse Interstitial Fibrosis of the Lungs", *Bull. Johns Hopk. Hosp.*, 74: 177.

HARRIS, M. S., PREUSS, F. S., GOLDMAN, A., and FRIEDMAN, N. (1957), "Cortisone Therapy in Hamman-Rich Syndrome. Report of a Case", *Amer. Rev. Tuberc.*, 76: 123.

HOFF, H. R. (1958), "The Hamman-Rich Syndrome. Review of the Literature and Report of a Case Treated with Prednisolone", *New Engl. J. Med.*, 259: 81.

OSWALD, N. C., and PARKINSON, T. (1949), "Honeycomb Lungs", *Quart. J. Med.*, 18: 1.

PEABODY, J. W., BUECHNER, H. A., and ANDERSON, A. E. (1953), "Hamman-Rich Syndrome. Analysis of Current Concepts and Report of Three Precipitous Deaths following Cortisone and Corticotrophin (A.C.T.H.) Withdrawal", *A.M.A. Arch. intern. Med.*, 92: 806.

PINNEY, C. T., and HARRIS, H. W. (1956), "Hamman-Rich Syndrome. Report of a Case Diagnosed Ante-Mortem by Lung Biopsy and Successfully Treated with Long-Term Cortisone Therapy", *Amer. J. Med.*, 20: 308.

READ, J. (1958), "Pathological Changes Produced by Anti-Lung Serum", *J. Path. Bact.*, 76: 403.

READ, J., and HOLLAND, R. A. B. (1959), "Hamman-Rich Syndrome Treated with Cortisone", *Thorax*, 14: 71.

ROSE, G. A., and SPENCER, H. (1957), "Polyarteritis Nodosa", *Quart. J. Med.*, 26: 43.

RUBIN, E. H., and LUBLINER, R. (1957), "The Hamman-Rich Syndrome. Review of the Literature and Analysis of Fifteen Cases", *Medicine (Baltimore)*, 36: 397.

SILVERMAN, J. J., and TALBOT, T. J. (1953), "Diffuse Interstitial Pulmonary Fibrosis Camouflaged by Hypermetabolism and Cardiac Failure: Ante-Mortem Diagnosis with Biopsy and Catheterisation Studies", *Ann. Intern. Med.*, 38: 1326.

TUFT, L., and GIRSH, L. S. (1958), "Diffuse Interstitial Pulmonary Fibrosis (Hamman-Rich Syndrome) in an Allergic Patient. Report of a Case", *Amer. J. med. Sci.*, 235: 60.

VAN SLYK, E. J. (1957), "Diffuse Interstitial Pulmonary Fibrosis (Hamman-Rich Syndrome) Diagnosed with Lung Biopsy; Treated with Cortico-Steroids", *Dis. Chest*, 31: 593.

WHITE, R. B., and CRAIGHEAD, J. T. (1957), "Hamman-Rich Syndrome (Diffuse Interstitial Pulmonary Fibrosis)", *Dis. Chest*, 31: 335.

Legends to Illustrations.

FIGURE III.—Case III: septal thickening. Alveoli contain œdema fluid. (×125.)

FIGURE IV.—Case IV: X-ray film of chest, showing coarse mottled opaque areas through both lung fields.

FIGURE V.—Case IV: septal thickening, cyst formation and cuboidal epithelial metaplasia. To be distinguished from ectatic bronchi. (×125.)

FIGURE VII.—Case VI: extensive fibrosis. A "concholdal" body is visible. (×125.)

FIGURE VIII.—Case IX, February 8, 1954: diffuse pulmonary infiltration, particularly in the right upper zone.

FIGURE IX.—Case IX, October 23, 1958: fibrosis and honeycombing.

A CASE OF RHESUS INCOMPATIBILITY OCCURRING IN A TWIN PREGNANCY.

By R. S. HYSLOP, M.B., B.S., AND W. WHILEY, M.B., B.S.,
Registrars, King George V Memorial Hospital, Sydney.

RHESUS INCOMPATIBILITY presents many problems, perhaps the greatest being the place of early induction of labour. Insufficient knowledge of the exact condition of the fœtus at the proposed time of induction has always posed the most difficult problem in management. Unnecessary and untimely interference often occurs when no direct measure of fœtal affection can be made, leading to the death of the neonate from prematurity alone. It has been found that (in our hands) serial estimation of maternal antibody levels does not offer a reliable indication of the severity of the hæmolytic process. Probably of more importance is the fact that antibody levels will not show sudden day-to-day or week-to-week alterations in the baby's intra-uterine environment, and thus the optimal time for induction of labour is lost. In the past, the indication for blind induction at 36 or 37 weeks has been a bad history of hæmolytic disease—that is, a previous pregnancy resulting in a severely affected baby or a death in utero from hydrops fœtalis. In an attempt to assess the presence and severity of the hæmolytic process in utero, the knowledge gained by Bevis (1956) in his spectrophotometric analyses of amniotic fluid has been applied.

An interesting case of hæmolytic disease in a twin pregnancy is presented to demonstrate the present management of rhesus incompatibility at this hospital.

Clinical Record.

A woman, aged 20 years, pregnant for the second time, was referred to the hospital when anti-Rh agglutinins were discovered at 28 weeks' gestation. Her blood was of Group A, Rh-negative, her last menstrual period had occurred on June 25, 1959, and her expected date of confinement was April 5, 1960. Estimations made by the Red Cross Blood Transfusion Service, N.S.W. Division, were as shown in Table I.

TABLE I.

Titre.	Saline.	Albumin.
Anti-D	16	64
Anti-C	4	16

Investigation of her husband's blood showed that it was of Group A, Rh-positive, R_1R_2 anti-C-positive. The probability of homozygosity in respect to the D antigen is 8:1. The patient's first pregnancy had been uncomplicated, and had resulted in a living male child born at term. No history of blood transfusion was elicited. She was first examined at 30 weeks' gestation, when the fundus was found to be at the height of 34 weeks. Palpation revealed a twin pregnancy, later confirmed by radiological examination. The pregnancy was normal in all other respects.

Amniotomy was performed on January 26, 1960, in a similar manner to that described by Bevis (1952). A point in the mid-line halfway between the pubic symphysis and the umbilicus was prepared with iodine and spirit, then infiltrated with 2 ml. of 0·5% lignocaine solution. A 19 gauge lumbar-puncture needle was then inserted into the amniotic cavity and 5 ml. of liquor were withdrawn. After centrifugation, the supernatant fluid was examined spectrophotometrically and the result plotted on a semilogarithmic graph. The result of this test indicated the presence of hæmolytic disease, at the time of only moderate severity.

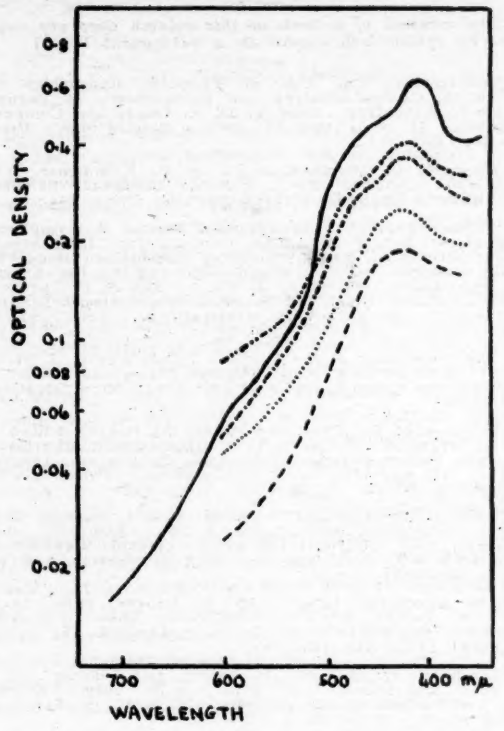


FIGURE I.

A further amniotomy was performed on February 9, and this test demonstrated an increase in the severity of the condition. The need for early induction of labour now became a distinct possibility, and with this object in mind it was held desirable to ascertain the degree of affection of each fœtus.

The information was obtained on February 16, in the following manner.

The first amniotomy was performed by introducing the needle 4 in. to the left of the mid-line and 2 in. below the umbilicus, and withdrawing the usual 5 ml. of fluid for examination. Two millilitres of Evans' Blue were then introduced into the amniotic cavity. After 20 minutes, to allow for mixing of the dye, a second puncture was made 4 in. to the right of the mid-line. As clear fluid was obtained, it was assumed that the other amniotic sac had been entered. Examination of these specimens revealed almost identical degrees of affection, and indicated an acceleration in the hæmolytic process. (See Figure I.)

At this stage it was thought that delivery within the next week was necessary to prevent a possible death in utero and to obtain babies in a salvageable condition. Vaginal examination with a view to induction of labour was performed on February 18. The cervix was found to be favourable with a breech presenting. During the same evening the patient came into spontaneous labour. At 2.30 a.m. on February 19, the first twin (a footling breech presentation) was delivered by the usual technique of Løvset manœuvre to the shoulders and application of forceps to the after-coming head. The second twin was spontaneously delivered by the vertex five minutes later. Blue liquor was aspirated from the pharynx of this baby.

The condition of the babies at birth was fair, but both were noticed to be pale and œdematous. The first twin weighed 4 lb. 7·25 oz. and the second 4 lb. 13·25 oz. Both gave a positive response to the direct Coombs test. Their subsequent progress is summarized in Table II.

TABLE II.[1]

Age.	Twin I.			Twin II.		
	Treatment.	Hb.	S.B.	Treatment.	Hb.	S.B.
Birth	(Cord blood.)	9·4	5		6·7	5·6
	Transfusion.			Transfusion.		
7 hours		15·2	9		15·5	14
	Transfusion.			Transfusion.		
31 hours			17			17
55 hours			29			27
	Transfusion.			Transfusion.		
79 hours			22			22
	Transfusion.			Transfusion.		
103 hours			19			20
127 hours			16			17

[1] Hb, hæmoglobin value (cord blood) in grammes per 100 ml.; S.B., serum bilirubin level in milligrammes per 100 ml. "Transfusion" means replacement transfusion of 80 ml. per lb. of body weight.

Discussion.

We believe that this case is an excellent demonstration of severe hæmolytic disease in a second pregnancy. Conventional management relies on the supposition that the first affected pregnancy usually results in a mildly affected baby. However, death in utero can occur, with disastrous results and a poor prognosis for further successful pregnancies.

Amniotomy and spectrophotometric analysis of the amniotic fluid give information as to the immediate status of the fœtus with regard to hæmolytic disease. With this knowledge, induction of labour can be undertaken with greater assurance and at the optimal time. When the results indicate that hæmolysis is progressing to the stage of severe anæmia and imminent hydrops, as in this case, one must be prepared to induce labour irrespective of the size of the baby or the period of gestation (here 33 weeks). Failure to do this will result in death in utero.

This case constitutes one of a series of cases of hæmolytic disease at present being studied at the King George V Memorial Hospital. It is hoped to publish full results and conclusions at a later date.

Acknowledgements.

We should like to thank Dr. A. Hobson, under whose care this patient was admitted to hospital, for permission to publish this case. The spectrophotometric analyses were made in the Queen Elizabeth II Research Institute for Mothers and Babies by kind permission of Professor B. T. Mayes.

References.

BEVIS, D. C. A. (1952), "The Antenatal Prediction of Hæmolytic Disease of the Newborn", *Lancet*, 1: 395.

BEVIS, D. C. A. (1956), "Blood Pigments in Hæmolytic Disease of the Newborn", *J. Obst. Gynæc. Brit. Emp.*, 63: 68.

Reviews.

Peripheral Vascular Diseases: An Objective Approach. By Travis Winsor, M.D., F.A.C.P., with a foreword by Burrell O. Raulston, M.D.; 1959. Springfield, Illinois and U.S.A.: Charles C. Thomas, Publisher. Oxford: Blackwell Scientific Publications, Limited. 9" x 6", pp. 866, with 435 illustrations. Price: £6 5s. (English).

THIS is an ambitious book of over 800 pages by a single author dealing with all aspects of peripheral vascular disease: physiology, investigational methods, pathology, clinical features and treatments. Although the book contains much of value and interest, particularly the sections on the various diagnostic techniques, there are certain disadvantages for the student or clinician.

It is not until well past the middle of the book (Chapter 28) that we reach a classification of peripheral vascular disease. Over 300 pages are devoted to investigational procedures (mostly requiring special equipment) and somewhat less than this to diseases. Space is given, not only to what are generally regarded as vascular diseases, but to other conditions, such as purpura (chapter 47), which are adequately discussed in text-books of general medicine. This space could be more usefully given to a fuller discussion of the more important peripheral vascular diseases proper, such as atherosclerosis, obliterans and thromboangiitis obliterans.

Generous use is made of diagrams. Although many of these are good and make their point, others seem redundant, only duplicating what is said in the text. Although schemata may be useful as *aides-mémoire* to students, critical readers would prefer actual photographs of clinical and pathological material.

The style is simple, but is sometimes rendered inelegant by inept expressions such as "spinal claudication" and "abdominal claudication" (page 412).

Some of the ideas are outmoded. In the chapter on anatomy and physiology of the sympathetic nervous system (Chapter 1), there is no mention of a vasomotor centre in the mid-brain. Considerable discussion is given to the theory of sympathin I and E, a theory developed before the discovery that the sympathetic transmitter substance is noradrenaline. The only type of aortography described (page 257) is the translumbar method, and of arteriography (page 260), the open method; these are now superseded by the more elegant and safer Seldinger technique and percutaneous arterography.

This book is recommended only to the critical reader able to sift the grain from the chaff.

Leprosy in Theory and Practice. Edited by R. G. Cochrane, M.D., Ch.B. (Glas.), F.R.C.P. (Lond.), D.T.M. and H.; with a foreword by Sir George McRobert, C.I.E., M.D. (Aberd.), F.R.C.P. (Lond.); 1959. Bristol: John Wright & Sons Limited. 9¾" × 6¼", pp. 424, with 189 illustrations. Price: 84s. (English).

DR. COCHRANE'S first book on leprosy, "A Practical Textbook of Leprosy", was published in 1947. During the following decade there have been many major advances in the field of leprology, notably the development of sulphone therapy, contributions to the pathology of leprosy by Khanolkar and others, and epidemiological and immunological studies by a number of workers. In this recent work the difficult task of describing adequately the theoretical and practical aspects of a complex disease has been well accomplished by the editor and a group of distinguished contributors.

The book, which contains a liberal bibliography, admirably fulfils its stated objective of being a guide, not only to workers in leprosy, but also to general practitioners in the tropics and elsewhere. It has, however, a wider range of appeal, since the study of leprosy impinges on many facets of research. Having regard to this fact, the editor has included authoritative contributions from specialists ranging from the basic sciences to orthopædic surgery.

A chapter devoted to recent studies of the sensory and neurohistological changes in leprosy is of special interest to the pathologist and the physiologist. The authors of this chapter have employed, for a dual purpose, the demonstration by Khanolkar of the affinity of leprosy for sensory cutaneous nerves. Their objectives were to explore the value of leprosy in studying the anatomy of cutaneous sensibility and, conversely, to apply recently developed neurological techniques to the histopathological study of leprosy. The results of investigation have been encouraging and merit further inquiry.

A discussion of the radiographic appearances and bone changes in leprosy is of interest both to the radiologist and to the clinician. In parallel with radiographic descriptions, the author evaluates causal agencies of the bony lesions of leprosy and defines the place of radiology in leprosy practice.

The book presents a fresh and stimulating approach to many of the problems in leprosy. It is an essential reference work for the leprologist and would be a valuable addition to the library of any physician interested in the disease.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"Oxosteroids: The Use of Phenolic Hydrazides for Detection, Characterisation and Estimation", by Bernard Camber, M.D.; 1960. London: H. K. Lewis and Company, Limited. 8½" × 5½", pp. 87, with 8 illustrations. Price: 12s. 6d. (English).

"Hypnosis in Anesthesiology", by M. J. Marmer, M.D., M.Sc.Med., (Anes.); 1959. Oxford: Blackwell Scientific Publications Limited. 9" x 6", pp. 166. Price: 54s.

"Oxygen Supply to the Human Fœtus: A Symposium Organized Jointly by The Council for International Organizations of Medical Sciences Established under the Joint Auspices of UNESCO and WHO and the Josiah Macy Jr. Foundation", edited by J. Walker and A. C. Turnbull; 1959. Oxford: Blackwell Scientific Publications Limited. 8⅝" × 5½", pp. 326, with illustrations. Price: 47s. 6d. (English).

"The Physiology of the Newborn Infant", by C. A. Smith, M.D.; third edition; 1960. Oxford: Blackwell Scientific Publications Limited. 9¼" × 6¼", pp. 600, with illustrations. Price: 95s.

"Diseases of the Chest—Including the Heart", edited by J. A. Myers, Ph.D., M.D.; 1959. Springfield: Charles C. Thomas, Oxford: Blackwell Scientific Publications Limited. 10¾" × 7", pp. 1026, with illustrations. Price: £13 16s. (English).

"Pediatric Neurosurgery", edited by I. J. Jackson, M.D., M.Sc., F.A.C.S., F.A.C.A., and R. K. Thompson, M.D., F.A.C.S.; 1959. Oxford: Blackwell Scientific Publications Limited. 10¼" × 6⅝", pp. 580, with illustrations. Price: £6 5s. (English).

"The Roots of Crime", by E. Glover, M.D., LL.D., Selected Papers on Psycho-Analysis, Volume 2; 1960. London: Imago Publishing Company Limited. 8½" × 5½", pp. 436. Price: 45s. (English).

"Biochemistry of Blood in Health and Disease", by I. Newton Kugelmass, M.D., Ph.D., Sc.D.; 1959. Oxford: Blackwell Scientific Publications. 10" x 7", pp. 544, with illustrations. Price: £6 6s. (English).

"The Student and Mental Health, An International View (The Proceedings of the First International Conference on Student Mental Health, Princeton, New Jersey, September 5-15, 1956)", edited by Daniel H. Funkenstein, M.D., Sponsored by the World Health Federation for Mental Health, International Association of Universities; 1959. London: H. K. Lewis and Company, Limited. 8½" × 5½", pp. 512. Price: £1 15s. (English).

"Biochemical Values in Clinical Medicine: The Results Following Pathological or Physiological Change", by Robert Duncan Eastham, B.A. (Cantab.), M.D. (Cantab.), D.C.O., Dipl. Path.; 1960. Bristol: John Wright & Sons, Limited. 7" x 4", pp. 148. Price: 15s. (English).

"Lipide Chemistry", by D. J. Hanahan; 1960. London, New York: John Wiley & Sons, Incorporated. 9" × 5⅝", pp. 340, with illustrations. Price: $10.00.

"Gestation: Transactions of the Fifth Conference, March 11, 12 and 13, 1958, Princeton, N.J.", edited by C. A. Villee, Ph.D.; 1959. Sponsored by the Josiah Macy Jr. Foundation, New York. 9" × 5⅝", pp. 262, with illustrations. Price: $5.75.

"The Practice of Clinical Child Psychology", by A. O. Ross, Ph.D.; 1959. New York, London: Grune and Stratton Ltd. 9" × 5⅝", pp. 286, with illustrations. Price not stated.

"Surgery of Repair as Applied to Hand Injuries", by B. K. Rank, C.M.G., M.S. (Melbourne), F.R.C.S. (England), F.R.A.C.S. and A. R. Wakefield, M.S. (Melbourne), F.R.C.S. (England), F.R.A.C.S., with a Foreword by Sir Gordon Gordon-Taylor, K.B.E., C.B., LL.D., Sc.D., F.R.C.S., F.R.C.S. (Ed.), F.R.A.C.S., F.A.C.S., F.R.C.S. (Canada); second edition; 1960. Edinburgh and London: E. & S. Livingstone Limited. 9¾" × 6¼", pp. 298, with 219 illustrations. Price: 45s. (English).

The Medical Journal of Australia

SATURDAY, APRIL 16, 1960.

THE WAITING PEOPLE.

SCATTERED throughout the modern world is a host of *homeless, stateless, purposeless people, refugees for* a variety of reasons—a million in Hong Kong, a million in *the Near East, one hundred thousand* in Europe, two hundred and twenty thousand in Tunisia and Morocco, *many more* in Central and Eastern Asia. That there should be no place where they are wanted for so many is a strange and damning commentary on the world in our day, especially in the face of great wealth and high standards of living in many countries, of vast technological development, of unprecedented international awareness and activity, and of vigorous development of ideals of human freedom and national self-determination. *It must* not be thought that all these people are sleeping without shelter under a frosty sky or *wandering over scorching* deserts, or that they starving or naked or wasted with disease. *Many do suffer in these ways, but many* more are provided for in one way or another in the matter *of shelter, food, clothing and some sort of medical* care. Their need is for something much more fundamental than *this, much more obvious and simple. They* ask of their fellow men what most of us take for granted—a country *and a home and something to live for.* They are waiting to be wanted. It is a reasonable plea, and to attempt to *answer it World Refugee Year* has come into being.

It would be easy to indulge in an emotional wallow over *this matter and achieve very little.* It needs more and other than this. *The Lancet*, in a report of a first-hand *survey of Europe's refugees in 1960*,[1] puts the position bluntly:

> It is all too easy to think and speak of refugees either, on the one hand, as units to be added to a statistical table or, on the other hand, in terms of emotional anecdotes. In fact, the refugee is an ordinary person in an extraordinary position: his need, like that of the next-door neighbour in trouble with his bank overdraft, is for informed and dispassionate advice and well-directed help. Each new refugee is an emergency; for the longer he is denied a full productive place in society, the harder will it be for him to take such a place—and incidentally, the heavier will be the charge on those who sustain him in unwilling idleness.

In other words, unless we deal with this situation promptly and adequately, whether from pure compassion or from enlightened self-interest, the world will face a heavy reckoning. Two primary needs are apparent—money and immigration opportunities. There appears to be no lack of organizations active in this field and well able to administer aid if resources are available. A great deal has been done by various United Nations agencies, by individual governments and by voluntary bodies of many kinds. However, more money than that at present available is needed if a sterile system of handouts is to be displaced by positive efforts at rehabilitation and the reestablishment of human dignity and life with some sense to it. It makes a call on the purses of both governments and individuals. Later this year, we understand, an appeal is to be launched in Australia for World Refugee Year, so the point need not be laboured just now; we shall come back to it.

The other need, that for immigration opportunities, may well be exercising our minds. *Australia has in fact done* a good deal in absorbing refugees and has now agreed to admit 13 suffering from *tuberculosis;*[2] *but we have no* grounds whatever for complacency or smugness. We are, in the over-all picture, *well off in this country. Our general* standard of living is perhaps unexcelled. Our potential is *great. Can we and other fortunate countries insist on* protecting our golden future at all costs to others, on *maintaining an extreme safety-first* immigration policy in the face of human misery and frustration outside our *boundaries? The question* is not just political, it has significant medical implications, and the pressure of *commonsense* medical opinion could strongly influence governments in their attitudes. From an informed medical viewpoint many immigration laws are, as *The Lancet* has said in an editorial article,[3] archaic, futile and harsh:

> *Their archaicism is evident from* their insistence on freedom from signs of pulmonary tuberculosis. *Their* futility is reflected in the experience of the Hungarian *exodus, when thousands* were allowed to cross borders with scant regard to security of medical checks: no country seems to have been endangered or put to *great expense.* Their harshness is shown by acceptance under them of the young and the fit *while their less* able relatives are excluded. Such negative selection *is not only* inhumane but also unfair: it is inhumane because it tends to split families, and *it is unfair* because it leaves the handicapped to the care of the *overburdened* first country of asylum. An early objective should be to secure that would-be *immigrants are* not considered as individual units, and that no family *is barred from immigration* simply because it has one or more disabled members: after all, no family need cost the second country of asylum anything if a *breadwinner can support his* relatives. One or two countries, recognizing this, have already gone some way towards amending their immigration laws.
>
> *Relaxation of these laws will not by itself* enable all the "hard core"—those who have been rejected for immigration under mass schemes—to settle in a second country. But *we should free our minds of any idea* that these people will necessarily be a burden on the community: impaired vision in one eye, loss of a kidney, an untreated hernia, a *healed tuberculous* lesion, a stiff knee—these barriers to immigration under mass schemes do not prevent useful work. On the other hand, the "hard core" also includes *some*—such as "unaccompanied" mothers with children—who will *less certainly be self-supporting.*

The *Lancet* suggests that priority should be given to the "unaccompanied" mothers with children, to the tuberculous and to the aging and elderly, and points out that the "hard core" people are not necessarily a burden on the country where they settle. In Norway, which has adopted a notably responsible attitude to this problem, 95% of this group are self-supporting.

We have quoted at length from *The Lancet* because of the importance of the subject and the honest way in which it is treated. Both the editorial and the report of the survey on which it is based are worth careful study. They refer, of course, almost exclusively to the needs of

[1] *Lancet*, 1960, 1: 481 (February 27).

[2] *The Sydney Morning Herald*, March 30, 1960.

[3] *Lancet*, 1960, 1: 475 (February 27).

Europe's waiting people, a problem which it is said can be solved and solved quickly if the right thing is done. Australia undoubtedly has a share in the responsibility for its solution. At the same time, however, if only by the accident of geography, we have to think of an even bigger problem—the millions of refugees to our immediate north. The problem is enormous and frightening, but it exists. Ignoring it will not solve it. Nor can we, like modern Canutes, hope to sweep it back disdainfully for ever from our golden beaches. Our contribution to its solution is really going to cost us something, and the sooner we make up our minds about this the better.

Current Comment.

PREDNISOLONE AND ASPIRIN IN RHEUMATOID ARTHRITIS.

THE Joint Committee of the Medical Research Council and Nuffield Foundation on Clinical Trials of Cortisone, ACTH, and Other Therapeutic Measures in Chronic Rheumatic Disease has presented a report[1] on a comparison of prednisolone with aspirin or other analgesics in the treatment of rheumatoid arthritis. It is noted that the results of previous trials conducted by the Joint Committee showed that there was little to choose between cortisone and aspirin in the long-term management of patients with rheumatoid arthritis, but that since then many analogues of cortisone have been introduced, of which prednisone and prednisolone appeared to be particularly suitable for the treatment of rheumatic diseases. Further trials were therefore initiated, and the results of a trial comparing the use of prednisone with that of cortisone in the long-term treatment of rheumatoid arthritis has already been published;[2] this demonstrated the superiority of prednisone over cortisone for this purpose. The latest trial was conducted on 84 patients of both sexes, between the ages of 17 and 59 years, who had a rheumatoid type of arthritis of from three to 24 months' duration. The general management of the patient in terms of rest, splintage, exercise and physiotherapy was that currently used in each participating centre. Within each centre one group of patients received prednisolone in an initial dosage of 20 mg. daily, which was subsequently adjusted on an individual basis to give maximum benefit. A second group was given aspirin or other analgesics. The results of the trial, which lasted for a period of two years, are set out in detail. It was found that the patients treated with prednisolone showed an early significant improvement in both clinical and laboratory indices of inflammatory polyarthritis, and that this improvement, though less marked, was still present to a significant extent at the end of two years. There was no significant change over the two years in the frequency of radiological signs of erosive joint disease in the hands and feet of those treated with prednisolone; on the other hand, in those treated with analgesics alone these signs showed a significant increase. A remarkable feature of the results of the trial was the fact that in many patients treated with prednisolone the agglutinating titre in the sheep-cell test rose during the two years of treatment, whereas such a rise occurred in only a few patients treated with analgesics. It is stated that this is an unexpected finding, since, in a previous study by J. H. Kellgren,[3] there was a positive correlation between high titres in the sheep-cell agglutination test and the extent of articular damage. This association was much less apparent in the prednisolone-treated patients in the Joint Committee's trial, and it is asked whether the process responsible for joint erosion may be not identical with that producing the rheumatoid serum factor, and whether prednisolone therapy may suppress the former while enhancing the latter.

On the question of dosage, it is stated that after two years of therapy the mean dosage was 10 mg. daily, which is still above the maximum of 9 mg. for men and 5 mg. for menopausal women recommended by C. H. Slocumb and his colleagues.[4] Out of eight patients in the trial who received 20 mg. of prednisolone daily for three months, four developed evidence of peptic ulceration and a fifth developed a psychosis—clearly an unacceptable incidence of complications.

In its conclusions the Joint Committee states that the administration of prednisolone for a period of two years, instead of or in addition to analgesics such as aspirin, will on the average improve the functional capacity and general well-being of patients so treated, and reduce the incidence of erosive joint damage. On the other hand, patients so treated are more likely to show a rise in sheep-cell agglutinating titre, and the significance of this, if any, for the patient's future is not known. A further conclusion is that if the daily dose of prednisolone approaches 20 mg. undesirable side effects are likely to occur, and that the highest acceptable daily dose for long-term treatment is probably in the region of 10 mg.

This report was presented at a meeting of the Heberden Society, and in the discussion which followed some concern was expressed as to the significance of the rising sheep-cell agglutinating titre, and the question was considered whether the results of this trial indicated that all patients with active rheumatoid arthritis should be treated with prednisolone. Two speakers put forward the opinion that steroids should be used only for severely affected patients and those in whom treatment with aspirin and other analgesics had failed. Professor Kellgren pointed out that all the hazards of long-term steroid therapy had not come out in the trial, and that the complete answer was not yet available and would require a trial and follow-up lasting 10 years. However, this authoritative report is evidently an important point of reference in any discussion on the treatment of rheumatoid arthritis and does give some general guidance to help in the choice of treatment for individual patients.

SCURVY AND ITS PREVENTION.

INFANTILE SCURVY is a topic which has received considerable attention in Australian pædiatric circles in the past couple of years, chiefly owing to the activity of Victorian pædiatricians, who were disturbed at the incidence of the disease in that State. At the meeting of the Australian Pædiatric Association last year, F. W. Clements[1] read a paper in which he discussed the question of whether ascorbic acid should be added to dried milk preparations, but concluded that this was doubtful, as to do so would be, in effect, to attempt to mask a failure in health education instead of remedying it. In the discussion which followed, speakers from Victoria seemed to favour the addition of vitamin C to dried milk, though it was pointed out that this would cover only a minority of the population, since many artificially fed infants were fed on boiled whole cow's milk.

Another recent contribution to this discussion is a paper by D. Grewar[2] of Winnipeg, in which he reports three cases in which infants with acute scurvy were treated by feeding with an evaporated milk preparation containing 5 mg. of ascorbic acid per ounce of the dry powder. No other source of vitamin supplement was given, but all three infants made a prompt recovery on this régime, though two of them required antibiotic treatment for intercurrent infections. Grewar states that the practicability of evaporated milk as an anti-

[1] *Ann. rheum. Dis.*, 1959, 18:173 (September).
[2] *Brit. med. J.*, 1957, 2:199 (July 27).
[3] *Brit. med. J.*, 1957, 1:850 (April 13).
[4] *Proc. Mayo Clin.*, 1957, 32:227 (May 1).
[1] MED. J. AUST., 1959, 2:800 (November 28).
[2] *Canad. med. Ass. J.*, 1959, 80:977 (June 15).

scorbutic vehicle is evident, and advocates the fortification of evaporated milk with vitamin C as standard practice as a realistic means of preventing infantile scurvy on the following grounds: (i) Breast-feeding is on the decline, and evaporated milk is widely used in artificial feeding. (ii) Overt infantile scurvy is endemic in several parts of Canada, and it is likely that there are many missed cases of scurvy in both its overt and its subclinical forms. (iii) The disease occurs for the most part in circumstances of ignorance and poverty, and the best efforts of public health authorities are often defeated by contrariness, lack of cooperation and inaccessibility. (iv) Geographical location and other factors often dictate the use of evaporated milk as a staple article of diet without supplementary sources of vitamin C; examples mentioned are Indian and Eskimo tribes, and elderly people living alone on tea, bread and milk. (v) The additional cost of the vitamin C fortification of evaporated milk is negligible; there are no contraindications, and no ill-effects from excess of it.

Australian conditions of course differ in some important respects from those in Canada. The long Canadian winter may well encourage a greater dependence on dried milk powder instead of fresh whole milk; it will certainly make the supply of fresh fruit nad vegetables more difficult than in this country. However, basically the question appears to be to what extent the community should accept responsibility for the few who through ignorance or incompetence will not look after themselves. Ideally it would certainly seem better to aim at educating every mother in the proper feeding of her children (since ignorance is, in the great majority of cases, the reason put forward for failure to give the infant vitamin-containing supplements), but it might be more practical to supplement the nation's milk supply with vitamin C to reach the few to whom good advice does not penetrate. On the other hand, it is also arguable that this is over-protection which, in the community as in the individual, may in the long run have a deleterious effect. Over-dependence on artificial aids can reach a point where the individual is encouraged to persist in faulty habits rather than attempt to change them. As Clement points out, the nursery is the place where the foundations for good dietetic habits can best be laid.

DARWIN'S ILLNESS.

SPECULATION as to the nature of the illnesses suffered by outstanding figures of previous generations is an intriguing sport, which exercises a great fascination especially for medical historians. Perhaps one of its virtues is that, as a general rule, such speculation can never reach finality. In a recent leader we made some reference to the fact that Charles Darwin's illness, which curtailed his activities for a great part of his adult life, is generally believed by medical critics to have been psychologically determined. This judgement has perhaps been prejudiced by the fact that the doctors who treated him at the time could find no physical basis for his symptoms and apparently concluded that he was a hypochondriac. We have recently come across an article by Professor S. Adler[1] in which the author puts forward a very plausible alternative hypothesis. Adler had newly returned from attending an international congress on Chagas's disease which was held at Rio de Janeiro last July, and with this background fresh in his mind, evolved the suggestion that it was this disease which made Darwin a chronic invalid for most of his adult life. Chagas's disease, or South American trypanosomiasis, is known to us only from textbooks of tropical medicine, for it is strictly confined to the American continent. However, in parts of South America it is very prevalent, and Adler states that in the province of Mendoza up to 60% of the population may give a positive result to complement-fixation tests for *Trypanosoma cruzi*, the causative organism. This trypanosome is spread mainly by the reduviid bug, *Triatoma infestans*, which has become adapted to human habitations and is a blood-sucking parasite of man and domestic animals throughout extensive regions in South America. In the areas where Chagas's disease is most prevalent up to 70% of these bugs may be found to be infected with the trypanosome. That Darwin was exposed to the risk of this infection there is very little doubt, for during his five years with H.M.S. *Beagle* he made extensive journeys in areas where it is still prevalent, and Adler quotes the following passage from Darwin's diary:

> We slept in the village of Luxan . . . in the province of Mendoza; . . . At night I experienced an attack (for it deserves no less name) of the Benchuca a species of Reduvius, the great black bug of the Pampas. It is most disgusting to feel soft wingless insects about one inch long crawling over one's body. Before sucking they are quite thin but afterwards they become rounded and bloated with blood, and in this state they are easily crushed.

Adler suggests that a purely psychological ætiology of Darwin's illness cannot be accepted as conclusive until all other factors have been eliminated. He goes on to state that it is obvious that all attempts to explain Darwin's symptoms must be based on a detailed analysis of the events recorded in the account of the voyage of the *Beagle*, as there is nothing of any medical significance prior to the voyage which could throw light on his subsequent illness. The last part of this statement is perhaps open to question, but Adler's quotation from Lady Barlow[2] certainly goes to the heart of the problem:

> Charles Darwin's forty years of invalid existence moreover were an unexpected sequel to his youthful vigour, for his strength and endurance were well above the average, as Captain Fitzroy has recorded in his account of the various incidents during the *Beagle* voyage.

Chagas's disease has received a great deal of attention from South American pathologists and clinicians, and there is a considerable literature on the subject. Adler states that particular attention has been paid to the clinical and pathological aspects of the myocarditis which appears in some victims of the disease, and that Darwin's exhaustion after physical effort can well be explained as a consequence of infection with *T. cruzi*. Adler also mentions that Brazilian clinicians maintain that Chagas's disease may cause symptoms related to the alimentary tract, quite apart from cardiac complications, though this is disputed.

It may therefore be accepted (i) that Darwin's symptoms can reasonably be regarded as being compatible with a diagnosis of Chagas's disease, and (ii) that he had ample opportunity of acquiring the infection. It is also easy to criticize some of the arguments put forward in favour of a psychogenic explanation of Darwin's symptoms. As Adler points out, chronic invalidism in the head of a family, whatever its cause, has psychological consequences, and is likely to evoke the protective instincts of his wife and an exaggerated preoccupation with illness in his children. However, Adler conveniently overlooks the symptoms of which Darwin complained while waiting in Plymouth before the *Beagle* set out on its famous voyage, and which Robert Platt[3] regards as a foreshadowing of his future invalidism. As we said at the beginning of this comment, it is not possible to reach any final conclusion, and the reader must be left to take his choice. Most will perhaps prefer to accept the explanation of psychological illness, which fits in so well with much else in Darwin's character and circumstances, but Professor Adler has at least offered us an attractive alternative hypothesis. Or is it only coincidence that the fiftieth anniversary of Carlos Chagas's discovery of the nature of the disease which now bears his name fell in the same year as the centenary of the publication of the *Origin of Species*?

[1] *Nature* (*Lond.*), 1959, 184:1102 (October 10).

[2] "The Autobiography of Charles Darwin. The First Complete Version edited by his Granddaughter", quoted by S. Adler, *loco citato*.

[3] *Med. Hist.*, 1959, 3:87 (April).

Abstracts from Medical Literature.

PÆDIATRICS.

Difficulty in Reading.

J. V. V. Nicholls (*Canad. med. Ass. J.*, September 1, 1959) discusses the management of children who have difficulty in reading, and emphasizes that many slow readers have superior intelligence and that few have ocular defects, though the intelligence should always be assessed and the eyes tested. Reading difficulties are ten times commoner in boys than in girls; this is possibly because girls generally learn to speak at a younger age than boys and have a larger vocabulary at school age. There is a close correlation between vocabulary and reading facility. In some cases crossed dominance may play a part in reading difficulty, the child having a poor sense of direction and tending to persist in mirror writing. By means of drawing exercises and hand-training exercises these children can rapidly be given a better sense of direction, and with it their mirror writing disappears. The child should be permitted to point out with the index finger of the master hand each word as he reads it, notwithstanding that school teachers dislike this. Remedial training classes have great value.

Congenital Heart Defects in Mongolism.

M. Liu and K. Corlett (*Arch. Dis. Childh.*, October, 1959) have studied congenital heart disease in a group of 173 mongoloid imbeciles admitted to the Fountain Hospital during a period of 14 years. Thirty-six per cent. of 44 patients who died and on whom autopsies were performed showed congenital heart defects. Of the 122 patients still in hospital, 9% have been proved to have congenital heart defects. The high proportion of maternal illness in the congenital heart defect group suggests that maternal health during pregnancy may have a direct bearing on the heart malformation. The result of the present survey agrees with a previous observation that persistent atrio-ventricularis communis is not the most common cardiac anomaly in mongolism in the age ranges studied, and supports the finding that ventricular septal defect is the most common, atrial septal defect the second, and patent ductus arteriosus the third in frequency. Other anomalies such as vessel anomalies, pulmonary stenosis, atrio-ventricularis communis, Eisenmenger's syndrome and Fallot's tetralogy are less common.

Testosterone-Induced Remission in Aplastic Anæmia.

N. Shahidi and L. Diamond (*A.M.A.J. Dis. Child.*, September, 1959) state that the treatment of aplastic anæmia in childhood and adolescence has been one of the most hopeless and discouraging problems in the practice of pædiatrics, and now it seems that this disease is increasing steadily in incidence. They describe a new approach to the therapy of aplastic anæmia. Five patients with severe bone marrow failure were treated with combined testosterone and corticosteroids. Remission occurred in all except one, who died from the simultaneous occurrence of gastro-intestinal bleeding and overwhelming infection. Even in this patient, however, the post-mortem examination of the bone marrow showed marked erythropoiesis. The bone marrow and peripheral blood studies in these patients revealed improvement beginning with early erythroid regeneration, then reticulocytosis with subsequent rise in hæmoglobin level. The beneficial effect of testosterone therapy was also noted on myelopoiesis. Concomitantly with the progress of the bone marrow and peripheral blood changes the patients showed remarkable clinical improvement. The rationale for this therapy was based on the erythrogenic effect of testosterone observed in patients under treatment for breast cancer and myeloid metaplasia.

Hyperbilirubinæmia without Iso-Immunization and Kernicterus.

A. Mores *et alii* (*Acta Paedit.*, November, 1959), in a study of 54 full-term and 170 premature infants, found that hyperbilirubinæmia without iso-immunization is more frequent than hyperbilirubinæmia resulting from iso-immunization, especially in premature infants. Its degree may even equal the latter, but the maximum level is usually reached as late as the fifth day, or even later. Damage to the central nervous system from hyperbilirubinæmia without iso-immunization has not been found in full-term infants. The number of cases of kernicterus associated with this condition in living premature infants or in premature infants seen at autopsy has not exceeded 1%. The authors believe that prophylactic exchange transfusion in full-term infants is useless, and that in premature infants it is theoretically unfounded and its practical value has not been proven. Thus if it is possible to exclude iso-immunization as a cause of hyperbilirubinæmia, and the presence or absence of iso-immunization can nearly always be determined after careful clinical, hæmatological and serological examination, hyperbilirubinæmia in full-term and premature infants may be allowed to follow its natural course.

Transient Synovitis of the Hip Joint in Children.

A. Spock (*Pediatrics*, December, 1959) reviews 47 cases of transient synovitis of the hip joint occurring in patients less than 14 years of age. Although allergic reactions and trauma have been postulated frequently as causative factors, the ætiology of transient synovitis is unknown. In this study evidence is presented to show that in four patients acute streptococcal infection was associated with the development of transient synovitis, and in another patient infection by Coxsackie B virus was present, which suggests that these agents may be among those ætiologically responsible for this syndrome. The disease has an acute onset, the predominant symptoms being limp, pain or both. Two-thirds of the patients have an upper respiratory tract infection and a slight elevation of temperature may be noted. All patients exhibit definite but varied restriction in passive motion of the involved hip joint. An obese or stocky physique probably predisposes a child to this disease. X-ray examination is not helpful in the diagnosis. Prevention of weight-bearing by bed rest until the patient is completely asymptomatic provides the best form of therapy, and failure to follow such treatment results in prolongation of the illness.

Beta-Hæmolytic Streptococcal Pharyngitis.

M. Stillerman *et alii* (*Pediatrics*, January, 1960) has evaluated the effectiveness of penicillin V, penicillin V potassium, benzathine penicillin G, erythromycin and tetracycline in eradicating beta-hæmolytic streptococci from the pharynx of 410 infected patients or carriers. The bacterial cure rate was 84% for 224 patients treated with benzathine penicillin G in combined doses. Of 23 patients treated with tetracycline 48% were cured. The data indicate that penicillin was definitely more effective than the other antibiotics, and that there was no significant difference in the effectiveness of the various types of penicillin used. The authors were impressed with the 15% relapse-and-failure rate in their patients despite administration of recommended regimens of penicillin, and found it difficult to determine whether a relapse was due to incomplete eradication of the organism or reinfection from household or environmental exposures. Acquired resistance of the microorganisms to penicillin and erythromycin did not appear to be responsible for the relapses and failures, since all the tested strains were sensitive to these antibiotics both before and after relapse.

Maple Syrup Urine Disease.

J. Dancis *et alii* (*Pediatrics*, January, 1960) describe another case of this familial disease which is characterized by central nervous system symptoms, a maple syrup odour to the urine, and an early fatal outcome. The male patient described lived for 20 months, the longest survival so far reported. There were increased amounts of leucine, isoleucine and valine in plasma and urine, indicating a block in the metabolic degradation of these amino acids. There was an accumulation in the urine of the respective keto acids, but not of the aldehydes or of the simple acids. This locates the block at a step common to all three amino acids, that of oxidative-decarboxylation. The alpha-hydroxy-acid derivatives of these amino acids are probably present, but the evidence is still incomplete.

Meconium Peritonitis.

A. Attramadal and K. Harnæs (*Acta Pædiat.*, September, 1959) state that meconium peritonitis, of which they report three cases, is regarded as an aseptic chemical peritonitis caused by the passage of sterile meconium into the peritoneal cavity through an intestinal perforation. In most cases a clear cause of the perforation can be found, obstruction of the bowel caused by intestinal atresia or stenosis, malrotation, meconium ileus, etc., being the most frequent causes. However, in some cases no cause of the intestinal perforation can be found. The condition manifests itself by signs of

intestinal obstruction, abdominal distension, bile-stained vomitus and delayed passage of meconium. If the intestinal perforation persists after birth, the infant will additionally develop signs of bacterial peritonitis. Signs of intestinal obstruction and possibly free gas and fluid in the peritoneal cavity may be demonstrated by radiography. Intraperitoneal calcifications can be revealed by X-ray examination in 75% of cases. The treatment of meconium peritonitis is surgical, the aim being to relieve the intestinal obstruction as well as to close any open perforation. The prognosis is poor, but surgical treatment may be successful.

PHYSIOLOGY.

Responses of the Australian Aboriginal to Exposure to Cold.

H. T. HAMMEL *et alii* (*J. appl. Physiol.*, July, 1959) report that measurements of thermal and metabolic responses of Central Australian aborigines exposed to moderate cold during sleep were repeated during summer and have shown that the small, but important, differences between these natives and control whites exist in summer to the same extent as in winter. The metabolism of the Central natives declined continually throughout the night. Without metabolic compensation, body temperatures of the Central natives fell at a greater rate than those of the whites. Measurements of thermal and metabolic responses of a mixed tribal group of tropical Australian aborigines under identical conditions of cold exposure have shown that the average tropical native was intermediate between Central natives and control whites. The metabolic rate for typical natives was 42·8 Calories per square metre per hour, compared with 48·7 Calories per square metre per hour for whites and 37·0 Calories per square metre per hour for Central natives. The authors suggest that the Australian aboriginal has an inborn ability to tolerate greater body cooling without metabolic compensation, which can be increased by prolonged exposure to cold.

Dietary Residues and Growth of the Large Gut.

J. F. MOINUDDIN AND H. WING-TSIT LEE (*Amer. J. Physiol.*, October, 1959) report that diets containing 67% cornstarch, or 42% cornstarch *plus* 25% lactose, agar, cellulose or raw potato starch, were fed to rats. Dimensions of the caecum and colon *plus* rectum, and many characteristics of large intestinal and fæcal residues were recorded. Possible relationships of these dimensions and characteristics to the diet-produced differences in weights of the cleaned caecum and colon *plus* rectum were sought by correlation and covariance methods. The following possible associations were found. The caecal dry weight was possibly associated with the length and maximum width of the caecum, when full, and also with the weight of caecal contents. The dry weight and the weight : length ratio of the colon *plus* rectum were possibly associated with the fresh weight of the fæcal pellet, and with other weights and dimensions of colonic contents and of fæces. Despite these findings, in most cases the authors could not decide what relationship the residues might have to large intestinal growth and function. Nor could they decide how certain diets stimulate caecal or colonic growth.

Upper Airway Obstruction in the Unconscious Patient.

P. SAFAR, L. A. ESCARRAGA AND F. CHANG (*J. appl. Physiol.*, September, 1959) report that airway patency was studied in 80 anæsthetized, spontaneously breathing patients, who received no muscle relaxants. With the neck flexed (chin towards chest), the airway was obstructed in all patients, in both the supine and prone positions, with and without an artificial oro-pharyngeal airway in place. With extension at the atlanto-occipital joint (chin up) in the supine position approximately 50% of the patients had an open airway. The other 50% required, in addition to extension of the neck, forward displacement of the mandible or the insertion of an oro-pharyngeal airway or both. Skiagrams demonstrated that the tongue is pushed against the posterior pharyngeal wall when the neck is flexed and the mandible is not held forward. The incidence and degree of obstruction were similar in the prone and supine positions, with comparable positions of the head, neck and mandible.

Heart Activity of Snakes during Diving.

K. JOHANSEN (*Amer. J. Physiol.*, September, 1959) reports that diving bradycardia has been demonstrated in a species of snake (*Tropidonotus natrix*). The bradycardia was developed rapidly and amounted to a reduction in heart rate of about 85%. The electrocardiographic findings revealed the slowing of the heart rate as affected mainly through a prolongation of the diastole, amounting to 30 times the pre-diving value. Duration of the electrical systole showed a prolongation of the *P-R* interval by 15% and the *Q-T* interval by 130%. A rapid and pronounced shift in the *T*-wave amplitude occurred upon submersion. The results suggest that the described *T*-wave shifts are due to changes in concentration of carbon dioxide in the organism. Increased concentrations of carbon dioxide in the respiration air induced bradycardia and had a depressant effect on respiration.

Lung Volume Restriction as a Ventilatory Stimulus.

J. C. MITHOEFER (*J. appl. Physiol.*, September, 1959) reports experiments on breath holding in man, which demonstrate that a restriction in the volume of gas in the lungs is an independent ventilatory stimulus which limits breath holding. This reflex stimulus interacts with the chemical stimuli from hypercapnia and hypoxia to determine the breaking point of breath holding. Previous work by others failed to demonstrate a relationship between lung volume restriction and hypoxia at the breaking point of breath holding with air. Experiments are presented which explain this and show that when hypoxia is present at the breaking point of breath holding, a time correction must be introduced to relate lung volume to the breaking point. When this is done, the relationship between lung volume restriction and hypoxia becomes apparent.

BIOCHEMISTRY.

Vitamin D.

J. MEYER *et alii* (*Arch. Biochem.*, April, 1959) have determined citrate synthesis from acetate and oxalacetate by tissue slices from rhachitic and control rats. No difference between kidney, liver, heart and gut was observed. Evidence for a vitamin D effect in cartilage was obtained. In comparison with the control specimens, the rhachitic tissue exhibited a general depression of citrate metabolism manifested by less endogenous citrate, which was utilized more slowly, and a diminished ability to synthesize citrate from its precursors.

Unsaturated Fatty Acids.

W. S. LYNN AND R. BROWN (*Arch. Biochem.*, April, 1959) have shown that small amounts of unsaturated fatty acids are oxidized to carbon dioxide, both *in vivo* and *in vitro*, at a greater rate than the corresponding saturated fatty acids. Fat-feeding to rats stimulates the rate of oxidation of unsaturated fatty acids. Cholesterol-feeding to rabbits, but not to rats, stimulates the oxidation of all fatty acids by mitochondria, especially unsaturated fatty acids. Long-chain unsaturated fatty acids are more readily activated by mitochondrial enzymes than most saturated acids.

Fluorine.

J. W. SUTTIL AND P. PHILLIPS (*Arch. Biochem.*, August, 1959) have shown that the rate and extent of skeletal fluorine retention in the rat are inversely correlated with age. Two distinct phases of fluorine deposition were apparent : a rapid retention extending over a few days, which is attributed to the ionic exchange of fluoride with the hydroxyapatite system, and a slower phase continuing for the remainder of the experiment, which was postulated to be due to the appearance of new exchangeable sites by recrystallization, and by osteoclastic and osteoblastic activity.

Cytochrome.

R. F. KAMPSCHMIDT *et alii* (*Arch. Biochem.*, May, 1959) have found that cytochrome *c* decreased progressively in the tissues of the rat bearing a Walker carcinosarcoma 256 as the tumour weight to body weight increased. Conditions which might be responsible for the lowered cytochrome *c* concentration, such as anæmia, low stores of iron, decreased muscular activity and inanition, were investigated. Decreased muscular activity, phenylhydrazine anæmia, and a combination of low iron stores and anæmia were found to lower the cytochrome *c* concentration in the tissues of the rat. None of these conditions, however, caused a sufficient decrease to be the factor responsible for the marked decrease that occurs in the tissues of rats bearing the Walker tumour.

Public Health.

SOME ASPECTS OF EPIDEMIOLOGY AND PREVENTIVE MEDICINE ABROAD.

The purpose of this report is to record certain observations and personal impressions arising out of a visit to Europe and North America during the period from March to September, 1959. The object of this visit was to examine methods being used in the prevention of disease, with special reference to the epidemiological approach. The inquiries which were undertaken were concerned more with principles than with details. They were, by force of circumstance, irregular and incomplete; but they included attendance at three international gatherings, several visits to various health departments and universities, and innumerable discussions with public health and other physicians, statisticians, microbiologists, epidemiologists and others associated with preventive medicine. The resultant polyglot of information has been arbitrarily rearranged for reasons of convenience, and individual topics are grouped according to the main inference of each. Some explanation of "the epidemiological approach" may be desirable at the outset, while an attempt will be made at the conclusion of the report to outline the future scope of epidemiology in relation to organized public health.

The Epidemiological Approach.

The three components of the word epidemiology—"epi", "demos" and "logos"—imply "a study of mankind's afflictions". This broad translation clearly requires expansion, and a number of unsuccessful attempts have been made to provide a comprehensive definition. The shorter definitions are inadequate, while the longer become unduly complicated. However, the one fundamental idea which all of them convey is that epidemiology has to do with communities rather than individuals. Use of the word was once restricted to epidemic or at least communicable disease. This is no longer true. It is now freely used in connexion with degenerative, traumatic and other non-communicable conditions. Here, then, is the second major implication of the word; and epidemiology is therefore concerned with any sickness, injury or disability which may afflict a community, regardless of cause.

The mainspring of epidemiological study is curiosity. The basic requirement is accurate data, and the essential technique is elementary statistical method. Curiosity is common. Accurate data are less common, but not rare, and can be collected in a variety of ways by many people. Some knowledge of elementary statistics is not hard to acquire. Epidemiology can therefore be applied by a wide range of people to a large field of subjects and for many different purposes. In the present situation, however, the main concern is with the wider public health problems, which at least appear to be controllable, if not preventible, while the special interests are the application of old epidemiological principles to the newer problems, and the development of fresh expedients.

The sense in which the term "epidemiological approach" is used for current purposes, therefore, is the exploitation of these concepts in studies of circumstances which are associated with the occurrence of sickness, injury or disability in a community, with the ultimate objective of attaining some measure of prevention or control.

The Community Survey.

One of the most profitable epidemiological techniques is that of the community survey, which is now being well exploited in Britain. It developed from a "chest" survey in a compact group of 30,000 people living in a Welsh valley, and began with an independent but comprehensive census of the entire community. From this background a recognizable morbidity pattern emerged, and the picture has since been clarified by a number of specific investigations. Analysis of material so accumulated has triggered off further supplementary studies, each designed to answer one of the many conundrums in medicine. Isolated rural communities in Australia offer good scope for this type of study.

A National Survey (the Canadian Sickness Survey).

This type of survey (of a national rather than a community character) provides information obtainable in no other way; but it is prohibitive in terms of labour and cost, and necessitates the use of elaborate statistical facilities. Further, the information gleaned, while being of great value from the administrative and planning viewpoints, is of restricted general interest. Among the multitude of findings in this immense study were the following. In Canada there is one disability per person per year. This lasts for approximately 11 days, of which about five are spent in hospital. The "under-fifteens" have more illness than others, and the commonest group of illnesses is respiratory. One in 27 persons has a surgical operation during the year. One out of every 17 people has a permanent disability. One-third of these people are in the working age-group (18 to 65 years).

The "Dove-Tail" Principle.

This principle is not new, but an ideal illustration of its special value is being provided by a London team investigating coronary disease. The several interlocking projects include a study of certification terminology, coronary pathology at incidental autopsies, and the relationship of physical activity, occupation, smoking habits, nutrition, heredity, hypertension and other factors known or suspected to have some influence on the disease. Not all diseases are amenable to this multilateral approach, and few teams are sufficiently well equipped to apply it, but it is a principle always worth bearing in mind whenever an epidemiological investigation is contemplated.

The "Serological Pattern".

The titration of pooled and "incidental" sera for antibodies of various types is a technique which has previously been employed in epidemiological investigation, and the New York City Health Laboratory has capitalized on its enormous "sera-for-WR" submission rate (700,000 a year) by "milking" all specimens for influenza-antibody tests ever since the Asian epidemic of 1957. Results have been plotted in terms of titre, time, and age-group—and in relation not only to the Asian strain, but also to the "FM1", "Lee" and "PR8" strains as well. The clear pattern of immunity so revealed would have been most difficult to disclose by other means, and is of great value in estimating the measure of hazard from epidemic influenza in various circumstances, and in indicating the relative need for the various individual antigens.

School Health Service (Reappraisal).

"Periodic school medical examinations have outlived their usefulness." The great majority of school-children are examined at least once a year by their family doctors. The old system should be replaced by a new one. This is the popular theme being pressed by a distinguished Canadian pædiatrician. It does not envisage dissolution of school services, but major reorientation. Suggested alternative arrangements include: (1) notification to the school medical officer of significant observations by the family doctor; (2) the conducting of special examinations only—for example, for hearing and vision—by the school medical officer; (3) medical *questionnaires* instead of medical examinations; (4) local committees and regular "staff meetings" to develop most profitable modifications. This crusade appears to have struck a receptive chord, and should lead to many reviews.

Tuberculosis Control.

The remarkable successes which have been achieved in the control of tuberculosis in various countries have led to a readjustment of old perspectives. One epidemiologist condemned the persistence of mass radiography as an unwarranted waste of technical resources, and suggested that its employment at the best should now be restricted to "high incidence" areas. In another advanced locality where the "Mantoux-positive" rate is now extremely low and where B.C.G. is not used, an observer remarked that "it would be as appropriate to use B.C.G. here in the prevention of tuberculosis, as it would be to use mass cholera vaccine" (cholera being non-existent there). These opinions are indicative of the reappraisal consequent upon epidemiological studies.

Rabies and Bats.

The occurrence of rabies in bats is provoking some concern in America. Not long ago a bat flew into a Manhattan apartment in daylight and died. Examination of its brain revealed "Negri bodies". How bats become infected is not clear. The fox, skunk and other animals have been incriminated as reservoirs in various States, but the potential role of the bat in spreading the virus is obvious. One veterinarian suggested that ordinary bats might become infected by contact with vampire bats in Central America and then migrate northwards. The

possibility of virus being introduced into Northern Australia by similar means seems remote, but worthy of contemplation.

Heart Disease.

The epidemiology of coronary disease is being energetically investigated in both Britain and America. Nutritional, occupational, genetic and other factors are all receiving attention, but the practical application of these studies is not yet clear. On the other hand, there is much organized effort designed to minimize the damage due to rheumatic fever. One epidemiologist made the following statement: "The value of routine medication in preventing recurrences and minimizing valve damage is now so well established, that the organization and surveillance of this should be a routine public health activity." Regular follow-up, free or at least cheap penicillin, work-evaluation and "special education for cardiacs" are some of the responsibilities which health organizations are accepting in partnership with clinicians or family doctors. State health services can make a useful contribution in this direction.

Hospital-Health Service Collaboration ("After-Care" Surveys).

The principle of hospital-health service collaboration is one whose application is of obvious value in reducing the total morbidity in a community. This principle is being developed notably in Scotland, where a series of surveys of patients discharged from hospitals (general, mental and geriatric) has disclosed a disturbing degree of deterioration in the condition of these patients in the absence of "effective organised after-care". Local "after-care" committees are being set up. Studies are being extended to identify "weak spots" which contribute to breakdowns subsequent to discharge from hospital, and the results will no doubt be profitable; this principle might well be extended in Australia.

"A.T.S." Reactions.

Until triple and quadruple antigen have "toxoid-protected" an entire generation, tetanus antiserum will continue to pose its special problem (with all its human, professional and medico-legal implications) and "sensitivity testing" will remain. A Canadian investigator reported at Edinburgh that several deaths from a "test-dose" of 0·1 ml. given intradermally had occurred, that "skin-test-doses" were of little value in identifying sensitivity, that the 0·1 ml. of a one in 10 dilution now used was safe but unreliable, and that adrenaline, antihistamines and the intravenous administration of "Solu-Cortef" (held readily available) were the best insurance. This is of little comfort in the face of records which show that at least 1% of reactions are dangerous, and some 5% generalized and severe.

Tetanus (Immunization Records).

There is universal concern about tetanus immunization records. Most health authorities encourage the maintenance of record cards, but their limitations are well realized. A metal disk (resembling that carried by active servicemen) has been proposed by some, tattooing by others. A few individuals in England already carry a "T" tattoo on their hips. Neither of these ideas is likely to gain wide popularity, although their advantages are clear.

Pharmacists and Public Health.

Pharmacists can be worthy participants in the campaign for better health. The potential value of the contributions they can make is illustrated by the two following observations. In one of America's largest cities, drug stores have accepted the role of "holding stations" for laboratory specimens; these are collected by laboratory trucks each evening. Only specimens for virus or "typhi" isolation are sent direct to the laboratory. In at least one American State the Pharmacists' Association has subsidized the "anti-poisoning" campaign by donating money for a poison control centre's initial library.

A Kit for Streptococcal Surveys.

Streptococcal surveys have hitherto been somewhat hampered by a cumbersome "throat-swab" technique. A Californian firm has overcome this inconvenience by putting out a small "strip-pack" (the "Cul-pak" kit) which eliminates the need for test-tubes and swab-sticks. The kit can be used by virtually unskilled personnel. It has been tried out in a preliminary study in Chicago City and found to be satisfactory. Streptococcal surveys are being carried out there as a complement to the "Rheumatic Heart Programme".

"Colicin-Typing" of Shigella Sonnei.

Dundee has many jute mills, employing many young mothers. The babies are left in nurseries during the day-time, and taken home to overcrowded tenements in the evening. Sonne dysentery is a recurrent problem in both nurseries and tenements. The source and path of spread are often difficult to trace. A technique of "strain-identification" (analogous to phage typing) is therefore being developed. It is called "the colicin technique". About a dozen Sonne types are now known to exist, of which four regularly occur in Dundee (type 7 being the commonest). This technique should be a useful aid in epidemiological investigation of outbreaks.

Blood-Sugar Machines and Diabetes Surveys.

Americans are concerned about undiagnosed diabetes. They consider that the morbidity and shortened life-expectation due to the unrecognized disease must be remedied. The early detection and stabilization of diabetics are therefore part of the official public health programme, and elaborate mechanical aids are being used in diabetic surveys. The most popular of these is a machine known as the "Clinitron", which resembles a large centrifuge in appearance and is capable of estimating many hundreds of "finger-prick blood-sugars" in a few hours. A more recent machine which undertakes multiple blood chemistry estimations is the "Technicon Auto-Analyser".

Accidental Poisoning and Poison Control Centres.

Accidental poisoning ranks high in the list of home accidents. The need to provide anxious parents and busy doctors with prompt information concerning the toxic components of proprietary preparations and the best course of action to follow in the event of accidental poisoning, has led to the formation of poison control centres or poison information bureaux. This type of swift information service is virtually confined at present to the North American continent. The first poison control centre there was probably that established in Chicago in 1953. Now there are over 200 of these centres in the U.S.A. and about 50 in Canada, with coordinating agencies in both Federal capitals. Some are located in health departments, others in hospitals. All seem to be popular with profession and public alike. They vary in form, personnel and manner of operation, but their basic structure and objectives are similar. All endeavour to provide a quick-answering service throughout the 24 hours of each day. Some centres deal with up to one episode per year per thousand people in the community which they serve. The majority of episodes involve small children, and the commonest poison is aspirin. The value of this type of service in saving life is obvious; but the opportunities it provides for follow-up and health education on a wide scale are even more important from the viewpoint of prevention.

"The Dry-Cleaners' Bag."

In America, garments are returned by dry-cleaners in very flimsy "Cellophane"-type bags. Because these bags are so light and transparent, children are strongly attracted to them, and are inclined to use them playfully as hoods. Owing to their delicate nature, and possibly because of an electro-static phenomenon, the material adheres tightly to nose and mouth. Little children find it very difficult to remove quickly. The result is, of course, tragic, for asphyxia follows. No less than 63 American children died from this cause during the first seven months of 1959. Clearly this menace warrants the widest publicity.

Road Accidents and Driver Tests.

In terms of "life-expectation" wastage, the accumulated toll from this cause outstrips all others. Few problems are more amenable to epidemiological investigation; yet few health investigators appear to be preoccupied with it. Of special interest, therefore, is a major study about to commence in Connecticut, where a "subject group" of 25,000 are to be investigated. With the aid of a specially equipped over-size caravan, detailed medical examinations are to be conducted. These will include tests of visual acuity, colour perception, visual fields and tonometry, urine examination, investigation of the blood chemistry, an electrocardiogram, and some psychological testing—apart from standard techniques. The aim is to reassess medical criteria for the issue of driving licences. Would that "driver-attitude" and emotional factors were to receive more attention!

Drug Addiction.

Despite every official embargo, the peddling of heroin flourishes, and the addiction problem persists. In one

North American city where addiction is of special concern, an investigation disclosed that the victims were physically "in good shape" despite long years of indulgence. Only the "demoralising" aspects were significant, and contributed to anti-social deterioration in various direction. Restrictive and punitive measures had proved ineffective, and a voluntary system of "unofficial" aid is being developed through a "foundation", which provides a hostel, a psychiatrist and skilled social workers. Coupled with realistic pilot studies, this offers some glimmer of hope.

Salmonellosis.

The extent of this problem is widely appreciated, especially in England. Because of its many complexities, public health administrators are frustrated by it, but microbiologists generally favour intensive comprehensive studies, including carrier surveys, egg checks, gland examinations, meat-meal tests, marker-swabs in abattoir outlets, general practitioner participation, and any other investigation which will help put the jig-saw pieces into place. At least 5% of Australian liquid egg is said to contain salmonellæ known to be pathogenic to man. Pasteurization of liquid egg is advancing, and an English firm has produced what is stated to be an effective pasteurizer. Bacteriological data were unobtainable.

Beach Pollution.

This is a man-made hazard, the extent of which is being belatedly recognized. Many parts of the English coast, the beaches of Lake Michigan, the shores of Lake Ontario and the inlets of Vancouver are all causing concern because of contamination by crude or partially-treated sewage. Nevertheless, none has apparently been incriminated in a typhoid outbreak as clearly as Western Australia's City Beach. The problem is being countered by regular bacteriological surveillance, intermittent beach closure, chlorination of effluent, and additional sewage-plant installations, while alternative long-term projects of a major nature are being developed as finances permit. May planners for the future profit from these mistakes of the past.

Allergy ("Pollen Studies").

Minneapolis is a city which is ringed by grain mills. There is an undue incidence of hay fever and asthma. This is readily demonstrable in "captive" groups, such as university undergraduates, of which there are many thousands. The Student Health Service is undertaking an epidemiological study of allergies to determine its precise incidence, pattern, evolution and relationship to the various pollens. The Botany Department carries out daily "pollen counts" (which are published, alongside the weather forecast, in the local paper). This type of study must be almost unique.

Fœtal Malformation and Viruses.

The prospective New York studies on rubella in pregnant women disclosed a fœtal hazard of approximately one in eight if the disease was contracted during the first trimester, and a similar measure of risk has now been recognized in Australia. The New York studies are being extended with the object of determining the precise influence of other viruses, while in Minneapolis the opportunity has been seized by investigating the effect of E.C.H.O. 9 virus on the fœtus by following the babies born of women involved in a recent widespread epidemic due to this virus. Including controls, the study group approaches 10,000. Controlled epidemiological studies of this kind must be of immeasurable value to smaller communities with fewer opportunities.

Poliomyelitis Immunization.

Since 1955, perhaps about 200,000,000 doses of Salk vaccine have been used in at least a dozen countries. This vaccine has come from at least eight different establishments. Vaccination rates vary widely, not only in the different countries, but in different parts of the same country. Generally, these rates have been highest among school-children. National rates are not readily available, because records are not everywhere complete. In Canada, the proportion of triply-vaccinated school-children is said to be 75%, and this would probably be true also of America as a whole. In Britain and most of Europe this proportion would be appreciably lower, although in selected localities it would exceed 90%. Among pre-school children rates are much lower, and three-dose figures of over 50% are rare. In the 19 to 40 years age group rates are lower still, and few countries include the "over-forties" in their vaccination programmes.

Post-vaccination experience has been surprisingly variable. In Canada and most of the major American centres, the use of the vaccine has approximated to the measure of protection observed in the original field trials; but in certain parts of America, Britain and Europe an undue number of fully vaccinated children appear to have contracted poliomyelitis. In these areas, while Salk vaccination is still official policy, there is an understandably keen interest in attenuated vaccines. This interest is even sharper in certain other countries where Salk vaccine has been difficult to obtain.

Production of Salk vaccine in Britain and Europe is being hampered by alternate antigenicity problems in respect of virus types I and III. These seem to be less conspicuous in North America, and vaccine production has advanced in this region to the point where the use of quadruple vaccine is rapidly becoming routine procedure. This vaccine has been used on a widespread scale in Canada for many months now, and the larger American cities will be using it in their regular programmes by the end of the year. The primary immunization course of quadruple vaccine involves four doses at the ages of three, four and five months, with a fourth seven to 18 months later. The general view among experienced public health men is that quadruple vaccination (incorporating inactivated poliomyelitis vaccine) should be the immunization sheet-anchor until the status of attenuated poliomyelitis vaccine has been clearly established.

Attenuated vaccines are being produced mainly at three centres in America, and experiments with these are being conducted on small scales in several States; but most of the oral vaccine so far has been administered outside America (but with the use of strains or preparations of American origin). Thus, nearly 10,000,000 doses altogether have been used in Russia, Nicaragua, Columbia and Costa Rica, while in the last-named country oral vaccination is the official national programme. Despite earlier misgivings in regard to mutation, most virologists are no longer apprehensive on this score, while the problem of "interviral interference" seems to have been exaggerated. Controlled trials hitherto conducted indicate that oral vaccination is not only safe and effective, but can also be used as a "reinforcer" of children previously immunized with killed vaccine. Nevertheless, wider and more varied trials will be necessary before oral vaccination can be generally accepted. These trials may occupy two or three years.

Immunization Practice.

Smallpox. Vaccination is encouraged through infant health centres and is advocated as early as the age of three months, although one authority claimed a 10% failure rate at this age and recommended waiting until six months. The proportion of schoolchildren vaccinated against smallpox appears to vary from 30% to 60% in various European and American communities.

Diphtheria-Pertussis-Tetanus. Immunization with triple antigen is more or less standard practice, but the type of material used varies. In Britain, where Salk vaccination is sub-maximal, many are still concerned with the hazard of "provocation poliomyelitis", and are disposed towards the alum-free preparations, despite their lesser antigenicity. In America and Canada, where circumstances are different, the use of alum toxoids is the rule. Primary immunization procedures are more or less uniform in respect to dosage and spacing, but "reinforcer" practice is highly variable. School-entry "boosters" are universal, but some interpose a pre-school or kindergarten one as well (although clear evidence of the need for this is lacking). A few recommended further "boosters" at the ages of seven and 10 years as well. The use of quadruple vaccine (or what the Canadians call "D.P.T. Polio") is rapidly developing into routine practice.

Poliomyelitis. The three-dose Salk schedule is orthodox, but in many places a fourth dose is being given one to three years after the third. Justification for this as a routine procedure is uncertain. One argument is that an immature infant may not respond adequately to three doses only; another is that immunity can wane. The case for it seems incomplete and only time and further observation will show whether it is essential. Attenuated oral vaccine is not yet officially endorsed in either Britain or America, although it is being used in limited trials in both countries.

Influenza. There is little enthusiasm for organized vaccination against influenza with a virus vaccine. The consensus of opinion is that any immunity following its use is partial, unpredictable and temporary, and the leaning is towards a specific vaccine for "special groups" at selected times.

Old Broad Street and Other Places.

Old Broad Street is now known as Broadwick Street, which is close to Piccadilly Circus. The Old Pump has gone, but its original location is marked by a brown kerbstone, which is distinguishable from the usual grey of London's pavements. Opposite this is the door of a public house which was recently renamed "The John Snow" and the sign overhead is a portrait of the celebrated epidemiologist. Inside the tavern are several framed newspaper clippings and other interesting exhibits connected with the cholera epidemic. There is also a visitors' book, in which there are at least four Australian signatures. Across the Circus, at 18 Sackville Street, a circular blue plaque identifies the place where Snow once lived; and at the Old Brompton Cemetery an impressive headstone has been erected over his grave.

In Bristol, the memory of another pioneer epidemiologist has been perpetuated by the establishment of a "William Budd Infant Health Centre". St. Peter's Hospital, where so many of his typhoid patients once lay, was razed to the ground during the "blitz". It is now a car-park. Alongside is the shell of St. Peter's Church. Budd's home is now George's Bookshop on Park Street.

Finally, in the heart of the beautiful Yorkshire dales there lies a comfortable cottage where a great general practitioner-epidemiologist now lives in retirement. Visitors to the home of William Pickles in Aysgarth are always welcome, and they will be regaled with fine sherry and many epidemiological anecdotes. Several Australians have made the pilgrimage to pay homage to this famous old man, to whom his visitors' book is a source of pride and joy.

Training in and Recruitment to Preventive Medicine.

Preventive medicine is not among the most attractive medical careers. As one distinguished American pointed out, "Not a single medical student enters upon his clinical years with any ambition to embrace preventive medicine, and few are attracted by it after graduation". The problem of recruiting capable young medical men is therefore one of the most important with which health organizations have to contend. Several American health departments and university departments of preventive medicine are endeavouring to stimulate the interest of young men in this direction by employing senior medical students (during university vacations) on special projects. Some have established residentships. A few have a bursary system, designed to help students through medical school in return for various services towards public health. These schemes have clear advantages. In the short run they help clarify the purpose and method of preventive medicine, while in the long run they must contribute to a better understanding and cooperation between clinicians and health departments. Whether recruitment is influenced or not, these schemes have obvious merit.

Epidemiology and Public Health.

Epidemiology was the seed from which the tree of organized public health grew, for it was the revelations of epidemiological studies which demonstrated the need for the creation of specific public health establishments. For many decades these establishments were preoccupied with communicable disease, and epidemiology remained a dominant activity within them. However, as the responsibilities of public health organizations expanded, many administrative branches developed. These, coupled with a progressive reduction in communicable disease, led to an overshadowing of epidemiology by the other (and now multifarious) public health activities. Two factors have probably been responsible for this. The first is the outdated concept that epidemiology is concerned only with communicable disease. The other is the increasing number of epidemiological investigations being conducted by academic and other research units outside the ambit of the conventional public health framework, and a growing tendency on the part of public health personnel to restrict their interests to the dwindling routine epidemiology, and to leave special projects to others. There seems to be a tendency towards neglecting the use of epidemiology in practical public halth, and a risk that the major instrument, which was formerly the "seeing eye", the "intelligence service" and the "ammunition provider" for public health departments, may rust away. If this was to happen, health departments would soon degenerate into automated bureaucracies, devoid of initiative or originality, and operating with limited effect behind a "Maginot Line".

On the other hand, if the epidemiological approach is fostered, and reapplied to the changing vista of public health, there is every hope that the indispensable role now occupied by public health departments will be enhanced and maintained for an indefinite era of time. The public health problem is no longer a matter of communicable pestilence. Questions of non-communicable diseases and social problems dominate the scene. These are no less amenable to epidemiological investigation than their communicable predecessors, and without investigation the answers to these questions will not be found. Public health departments are equipped by experience, tradition and organization to exploit the possibilities of epidemiology more effectively than any other agency: but they need the leadership, inspiration, drive and support of their directors if this is to be accomplished.

Development of this branch of public health offers the best prospect of keeping health organizations in step with changes in the present and future. It is in the interests, not only of these organizations, but also of the community, that this should be widely recognized.

D. J. R. SNOW.

Director of Epidemiology,
Department of Public Health,
Perth, Western Australia.

British Medical Association.

VICTORIAN BRANCH.

A Dinner to Dr. H. Cecil Colville.

A PLEASANT FUNCTION was held at the Union House, University of Melbourne, on November 23, 1959, when the Council of the Victorian Branch of the British Medical Association and the Committee of the Medical Society of Victoria entertained Dr. H. Cecil Colville at dinner and presented him with a miniature of his portrait painted by Mr. W. Dargie. The President of the Branch, Dr. J. Gavin Johnson, presided. The guests included a number of past-presidents of the Victorian Branch, the Vice-President of the Federal Council, Dr. A. J. Murray, the General Secretary of the Federal Council, Dr. J. G. Hunter, the Editor of THE MEDICAL JOURNAL OF AUSTRALIA, Dr. R. R. Winton, and Mr. W. Dargie. Dr. David Roseby proposed the health of Dr. Colville, who has been Chairman of the Council of the Victorian Branch since 1939 and President of the Federal Council since 1955.

The occasion was also taken to honour the two oldest members of the Victorian Branch Council, Dr. F. L. Davies and Dr. J. P. Major. Their health was proposed by Dr. Gerald Weigall.

Presentation of Portrait of Dr. H. C. Colville.

On December 4, 1959, at a function held at the Medical Society Hall, East Melbourne, a portrait of Dr. H. C. Colville which had been commissioned by the Victorian Branch of the British Medical Association and the Medical Society of Victoria and painted by Mr. William Dargie, was presented to the Council. The presentation was made by His Excellency the Governor of Victoria, Sir Dallas Brooks.

Dr. H. G. Judkins, the President, in welcoming his Excellency the Governor, Sir Dallas Brooks, and Lady Brooks, said that the occasion was an historical one for the Association in Victoria. Members were duly conscious of the honour paid to the Branch by the presence of His Excellency to present the portrait of Dr. Colville. It was many years since the Council had commissioned an artist to paint a portrait of any of its outstanding leaders, and there was none which would hold a more honoured place than that of Henry Cecil Colville.

The President then read the following citation:

> Among those who have rendered signal service to the medical profession and to the British Medical Association in Australia, the name of Henry Cecil Colville, M.B., B.S., F.R.A.C.S., stands high.
>
> He was first elected to the Branch Council in 1928 and has been continuously a member since then, being appointed a Trustee of the Medical Society of Victoria in 1947. Dr. Colville has been Chairman of the Branch Council since 1939 and was President of the Branch in 1940.
>
> In 1939 he was elected to represent the Branch on the Federal Council of the British Medical Association in Australia and, with the exception of the year 1946 (when he did not stand for election), has remained a member of that body, being appointed its President in 1955.

The President concluded by saying that Dr. Colville's many friends had felt that the time had come when his services to the medical profession should in some degree be recognized by the painting of his portrait. That had now been done by Mr. William Dargie. The President then asked His Excellency, on behalf of contributors, to present the portrait of Dr. Colville to the Victorian Branch of the British Medical Association.

Sir Dallas Brooks thanked the President for his words of welcome to Lady Brooks and himself. He referred to the signal service rendered to the medical profession by Dr. Colville, and to the importance of the British Medical Association to the profession. He said that Her Majesty the Queen, as Patron of the Association, would no doubt wish to add her tribute of praise and thanks to Dr. Colville; as her representative he offered him congratulations and thanks. He commended the action of the Victorian Branch of the British Medical Association and the Medical Society of Victoria in commissioning Mr. William Dargie to paint the portrait. Sir Dallas Brooks then unveiled the portrait and handed it to the President for safe keeping.

Dr. Colville, in reply, said that it would be difficult to recall how many times he had stood on the platform in the hall and addressed a gathering, but on the present occasion he was faced with a situation for which all that experience provided him with no precedent, and he found it very hard to know how to cope with it. He thanked His Excellency and Lady Brooks for coming and making the presentation. He said that in doing so they had conferred a great compliment on him personally, and on the whole of the medical profession, which he represented. Dr. Colville said that His Excellency had not visited the headquarters of the Victorian Branch before, but it was the sincere wish of his Council and himself that this first visit would not be his last.

Dr. Colville then thanked those who had made the presentation possible and those who had come to the presentation. One of the rewards of the position he held was that he met so many of his colleagues and had the opportunity of making real and lasting friendships. He wanted all those present to know how much he appreciated the gesture and how thrilling it was for him to see them all.

Dr. Colville then thanked Mr. Dargie. He said that he had thoroughly enjoyed the sittings for the portrait, partly because it was an unusual experience for any medical man to have not only the opportunity, but the obligation, to sit perfectly still for two hours and do nothing. There was no need for him to say anything about the portrait—it spoke for itself; but he felt that it was a great honour to have been the subject of what he thought everyone would agree was a masterpiece of the portrait painter s art.

Dr. Colville then thanked the members of the Council, who had borne with him and given him great support over the last twenty-one years. They had not only instigated and carried out the arrangements for the painting of the portrait, but they had also reelected him to the position of chairman. For that he was very grateful and he looked forward to a further period of interesting work associated with them. Those twenty-one years had been an interesting and enjoyable time for him. Everyone had heard the B.M.A. described as a "closed trade union". Admittedly the Association did try to look after the interests of its members, but in doing so it also looked after the interests of the public, whom it was the duty of the profession to serve. He had always maintained that a good medical service could be provided only by doctors who were working in congenial circumstances and entirely free from any feeling of dissatisfaction or discontent with their conditions. He thought that, as far as Victoria was concerned, doctors enjoyed those conditions, and it was something more than a coincidence that as a result the standard of medical service, of scientific endeavour and of research in Victoria ranked very high and, according to overseas visitors, compared very favourably with that in any other part of the world. He could only say that, as long as he had any position of responsibility in the Association, it would be his endeavour to see that those conditions were maintained. He did not want to leave the subject of members of Council without saying a word of thanks to members wives, and perhaps in particular to his own wife. Everyone had heard of "golf widows" and "fishing widows"; but to his mind the greatest sufferers of the lot were "B.M.A. widows", since many meetings went on after midnight.

In conclusion, Dr. Colville said that it would be a great source of pleasure and pride to him that the portrait would hang in the Council Chamber opposite that of a very distinguished past member of the Association, Crawford Henry Mollison, who had established, probably for all time, the record of service on the Council of 51 years. With his own modest record of 31 years, between them their records represented 82 years of service to the Association. He hoped that the presence of those two portraits in the Council Chamber in the years to come might act in some way as a stimulant and inspiration to future members of the Council, and concluded his remarks by expressing his gratitude for the nicest thing that had ever happened to him.

Out of the Past.

A TRAGIC DEATH.[1]

[From the *Australasian Medical Gazette*, October, 1899.]

THE tragic death of Dr. E. P. Vines at Braeside Station W.A. in September whilst attending Mrs. Hodgson the wife of the proprietor forms an instance of one of the many perils still attending the practice of our profession. A number of aborigines attacked the homestead before day break. Mr. Hodgson was sleeping outside the building with one of his children. He was awakened by the barking of the dogs. He sat up and was immediately speared in the shoulder. He shouted to his wife and Dr. Vines that the natives were attacking them, and at the same time received other spear wounds. Dr. Vines ran out and received two spear wounds, one of which wounded the heart. He turned into the house, and exclaimed "I'm done" and immediately expired. The patient got out of bed, took a revolver, and fired at the natives, who thereupon decamped. This plucky act of the patient saved the lives of all others of the household. She subsequently gave birth to a son. We cannot bestow too much sympathy, encouragement, and praise upon those of us who carry out their life work in the back blocks and distant parts, far removed from help and civilisation. It can truthfully be said of Dr. Vines that he died in the execution of his duty —one of the highest privileges to which mortal man can aspire.

Special Correspondence.

PARIS LETTER.

FROM OUR SPECIAL CORRESPONDENT.

Electronics and Medicine.

AMONGST medical activities in Paris in May and June, 1959, an important event was the holding at the UNESCO offices of the second International Conference on Medical Electronics.

At the instigation of the Rockefeller Foundation, and with the assistance of the Council for International Organizations of the Medical Sciences, a first international conference on medical electronics had been held in 1958 at Paris, from June 26 to 28; it was a rather timid first attempt before a fairly limited audience, marking the first appearance of this new medical group. In 1959, the second conference had much greater scope and assurance; moreover, such an opportunity for the exchange of points of view and of techniques is certainly indispensable. For, if medicine has gone as far as it can—or almost as far—in clinical research as was thought possible at the turn of the century, associated fields of investigation, assisted by the remarkable progress that has been made in techniques of all types, are at present only in their very early stages.

The hand and mind of the doctor—which cannot be replaced—are now extended by electronic brains, by radioactive particles which penetrate the very inmost parts of the cells, and which scintillation counters detect with precision by means of cathode tubes in which electrical impulses are recorded in luminous tracings, etc.

There is no doubt that the medical practitioner, although he has reasonable scientific equipment, feels a little left behind by the technicalities of these new investigations and their complexity. Electronics are everywhere, and the

[1] From the original in the Mitchell Library, Sydney.

problems that arise are as much problems in physics and mathematics as actual medical problems. However, some of the results already achieved are so exciting that it is impossible to do anything but concede the necessity for an alliance between electronics and medicine, which implies close cooperation between doctors and electronic engineers.

It is not possible in this place to report in detail all the communications presented to the conference. A large number of them are so technical as to be rather tedious for the uninitiated. We shall simply try—with a few examples—to pick out some of the principal problems studied; as we shall see, these are very varied.

The electroencephalographic research that was reported was extremely interesting, even if it was not particularly spectacular. Electronic apparatus has been used to obtain a spatio-temporal picture of the electrical activity of the brain. The varying potentials of the numerous electrodes arranged about the scalp can be coordinated only by complex electrical circuits. Frequency analysers separate the different frequencies in one tracing, and the curves produced by these analyses can then be used in an electronic calculator.

Electrooculography makes possible the objective recognition of hemianopsia, partial colour blindness, cerebellar syndromes, etc., by recording abnormal movements of the eyes. Pulmonary investigation may also find a use for electronics. Variations in the lighting up of a photoelectric cell receiving the light from an X-ray screen can reveal, either the blood flow and the pulsations of the pulmonary blood vessels, or the pulmonary ventilation. Cinedensigraphy and steatidensigraphy thus make it possible to study without catheterization the localized pulsations of the pulmonary arterioles and even the oxygen consumption of a lung.

Investigation of the digestive tract may possibly one day benefit from transmitters in the form of pills (little marvels of construction in miniature) which automatically transmit the pressure, pH and temperature of the regions through which they pass.

Equally dramatic are the "spare hearts"—electronic stimulators of the beating of a sick heart which cannot alone maintain the regularity of its beats. These "pacemakers", as our Anglo-Saxon colleagues call them, consist of tiny electrodes which set the beats going, and a piece of apparatus which is partly inside and partly outside the body, and which sets off the electric discharge. Induction phenomena are used to make the electricity flow from the generator outside the body to the receiver inside it. Many technical problems have been raised, but they seem to a great extent to have been solved.

Open heart operations also require the aid of many electronic electrical mechanisms. The supervision of such delicate procedures, requiring a dozen or so technicians, calls for constant cathode-tube electrocardiography, electroencephalography, supervision of arterial and venous blood pressure by electromanometric means, constant pH measurements to indicate acid-base equilibrium, etc. The electrical defibrillator is also an item of the equipment of the operating theatre. In fact, there is no field of medicine to which electronic instruments cannot lend themselves, with all their concomitant advantages.

It has been possible to put into practice in the laboratory electronic methods of determining the sensitivity of bacteria to antibiotics, by measuring the changes in oxygen-reducing potential of a broth culture, and to develop automatic scanners of cell smears which preselect abnormal cells for cancer diagnosis and far surpass automatic red-cell counters. Space doctors are occupied with the transmission to observers on earch of the physiological information gained from animals propelled into space by rockets. Perhaps the orthopædic surgeons will soon perfect artificial limbs to be worked by the potential electrical power which persists in injured muscle groups. Obstetricians will be able to detect the presence of twins by means of electrical readings, avoiding the radiation hazards of pelvic radiography.

Electronic science has not reached as far as medical diagnosis itself, the logical aspect of which has not been studied to analyse how far electronic mechanisms could do duty for certain phases of this intellectual process.

This brief review of some of the interesting facets of the second medical electronics conference obviously does not touch on a number of more or less technical topics. But it is possible to say with assurance that all fields of medical activity and medical research benefit, or will benefit, from this wonderful tool which the displacement of electrons provides, and which, frequently, being more sensitive than our senses and quicker than the mind, although still flexible and tractable, makes all kinds of bold ventures possible.

A New Method of Aortography.

Aortography is not a simple and safe procedure. Therefore F. Pinet and his colleagues[1] have been considering a method which employs neither the venous route, with its numerous inadequacies and failures, nor the arterial route (by direct puncture of the aorta, by puncture of the left ventricle or by injection into the branches of the aorta) which is not free from serious risk. These workers employ injection of a peripheral artery (most often the radial artery), into which, by means of a trocar, the contrast medium is injected against the direction of blood flow; this, owing to the previous administration of an efficient, short-acting hypotensive drug (in this instance, trimetephane camphosulphonate, marketed under the name of "Arfonad"), flows back along the aorta and its branches. General anæsthesia is useful in suppressing subjective discomfort; hypotension after perfusion of this drug is of very short duration, lasting about five minutes, and owing to the lowered blood pressure it is possible to use a minimum quantity of contrast medium (20 to 30 ml.). The pictures gained by this technique are notable for the particularly clear contrast in the filling of the aorta and the quality of arteriolar detail.

The Syndrome of Laceration of the Broad Ligament.

After observing 30 cases of this specific syndrome, described by Masters and Allen, J. Varangot and his coworkers[2] describe the condition in general terms. The trauma is a laceration of the posterior layer of the broad ligament, usually obstetrical in origin. Ætiologically, the injury is caused by the trauma of a difficult or abnormally rapid labour, as also by that of uterine curettage after miscarriage. The clinical picture is one of retroversion of a uterus with an abnormally mobile cervix, accompanied by a string of functional symptoms, of which the chief are pelvic-abdominal pains, dyspareunia, dysmenorrhœa and asthenia, and which date from the gynæcological trauma. Anatomically, there is a unilateral, or most often a bilateral, tear of the posterior aspect of the broad ligament, involving the peritoneal layer or the underlying fascia, situated on each side of the isthmus, often in association with a large varicocele of the uterine vessels and a quantity of serous liquid in the recto-uterine pouch. Treatment is surgical and repair is simple, the two planes of the breach being brought together in a type of ligamentopexy procedure.

Cardio-Vascular Complications of Typhoid Fever and Disturbances of Cell Metabolism.

According to a detailed physiopathological study by J. Thiodet and his colleagues,[3] the origins of the cardiovascular complications of typhoid fever are to be sought in investigations of the metabolism of cardiac muscle cells. The myocardial condition in typhoid fever is metabolic myocardosis in which potassium is largely concerned. We must be able to anticipate these cardio-vascular complications, whose frequency dose not seem to have been affected by modern therapeutics. The best means of preventing these disturbances lies in appropriate rehydration, with an adequate contribution of energizing agents and potassium to prevent cellular exhaustion, and in the case of severe sympathetic disturbance the use of nerve-paralysing agents after the method of Reilly. In the event of cardio-vascular collapse, indicating complete cellular exhaustion, one must not rush in with sympathomimetics, the major cardiotonics or cortisone, with its not only useless but detrimental effects; one must recharge the muscle cell by means of hypertonic glucose solution and serum, potassium, insulin and strychnine in large doses, and this action is often enough. Once the cell has been recharged and the membrane potential restored, it is sufficient to administer small doses of sympathomimetics, if necessary, to achieve a complete cure.

The Infectious Arthritides after Intraarticular Injection of Cortisone.

The increasingly frequent administration of these intra-articular injections, which are often effective in the treatment of painful articular lesions, is not without some danger. J. and R. Judet[4] warn against the more frequent occurrence of infectious arthritides after intra-articular injections of hydrocortisone. Some of these joint

[1] Pinet, F., Gravier, J., and Pinet, A. (1959), *Sem. Hôp. Paris*, 35 : 1855.
[2] Varangot, J., Granjon, A., Chartier, N., and Loffredo, V. (1959), *Presse méd.*, 67 : 1139.
[3] Thiodet, J., Fourrier, A., and Arroyo, H. (1959), *Presse méd.*, 67 : 1305.
[4] Judet, R., and Judet, J. (1959), *Concours méd.*, 81 : 3069.

lesions are chronic and subacute, and their infectious character may not be appreciated. On other occasions, one is faced with a very severe reaction and acute symptoms. Once the inflammation has been relieved, penicillin therapy must be undertaken in massive doses. When a collection of pus is noticed, it must be released by arthrotomy; then plaster immobilization or continuous extension must be employed for some days. As soon as the signs of inflammation have disappeared clinically and biologically, mobilization is cautiously begun. The seriousness of these incidents is a reminder that this technique, which is becoming more and more common in the practitioner's surgery, must be a strictly aseptic one; it is a serious surgical procedure which must be accompanied by full rigorous precautions, in order to avoid these incidents and their grave sequelæ.

A New Method of Treating Barbiturate Coma.

Professor P. Mollaret and his co-workers[5] have attempted to treat barbiturate coma by a completely new method—alkalization of the plasma. The modern treatment of barbiturate coma entails conforming to a detailed régime of constant supervision of clinical and humoral factors, and of vigilant resuscitation of both the respiratory system and the circulatory system, but the use of these methods means that the patient must wait until the ingested poison is excreted normally. P. Mollaret and his colleagues wished to speed up this excretion. In order to hasten renal elimination of the toxic substance they made use of the principle of alkalization, and their experiments with animals showed that as a result of alkalization of the plasma, phenobarbital was freed from the cells by the raising of the blood pH, and excreted in increased amounts by the kidney, owing to the raised pH of the urine. The clinical application of this method is as follows. In cases in which neither intubation nor tracheotomy has been performed, alkalization is carried out by simple infusion of an isotonic bicarbonate solution (14%) in an average quantity of three to four litres per 24 hours. Polyuria causes very rapid excretion of the toxic substance. In patients who have previously undergone intubation or tracheotomy, alkalization is achieved by infusion of a hypertonic bicarbonate solution (30%). The conditions for the application of this method are unimpaired renal function, the necessity to maintain the systolic blood pressure above 100 mm. of mercury, adequate provision of potassium and calories, and, finally, constant biological supervision. Fifty-seven patients have been treated by this method, and all have been completely cured, with an appreciable reduction in the duration of coma.

Trial of Posterior Pituitary Hormone in Aerosol Form During Labour.

Administration of 10 to 15 units of the oxytocic principle of the posterior lobe of the pituitary gland (oxytocin) for 15 minutes in aerosol form has been tried by A. Notter,[6] who reports 80% positive results in the minor degrees of uterine inertia in six primiparæ and 14 multiparæ. No difficulty was recorded with either mothers or children. Greater consistency in the positive results would be more likely to occur with improvement of the apparatus to enable it to atomize micellæ of uniform diameter, less than 0·05μ. Improvement in methods of atomization should allow this procedure to be applied safely in clinical practice, for example, in the induction of labour in combination with intermittent oxygen therapy.

Physiology and Treatment of Senile Osteopathy.

According to A. Lichtwitz and his co-workers,[7] senile osteopathy is linked in the majority of cases with alteration in the organic matrix of the bone, rarely with isolated calcium and phosphorus deficiencies, but frequently with osteoporosis and osteomalacia. Changes in the organic matrix depend on known glandular, metabolic and tissue factors, but calcium deficiency often goes unrecognized. When it is associated with osteoporosis, it is the result of two processes usually uncommon in old people—renal glomerular insufficiency, without azotæmia, and reduction in the gastric flow of hydrochloric acid. Bone-forming treatments alone present difficulties on occasion, for it is always possible to mineralize a skeleton by the administration of vitamin D, provided that it is adequately supplied with organic matrix. Therefore, the therapeutic programme for an osteopathic condition requires classical metabolic therapy (adequate protein), tissue therapy (kinetotherapy, relief of pain), and glandular therapy (œstrone and testosterone in combination), combined with the administration of non-virilizing androgens and, in obstinate cases, of œstrogens in massive doses, and stimulation of the parathyroid glands by sudden deprivation of calcium aided by the intermittent administration of sodium phytate.

[5] Mollaret, P., Rapin, M., Pocidalo, J.-J., and Monsallier, J.-F. (1959), *Presse méd.*, 67: 1435.
[6] Notter, A. (1959), *Presse méd.*, 67: 1479.
[7] Lichtwitz, A., de Seze, S., Hioco, D., and Bordier, P. (1959), *Sem. Hôp. Paris*, 35: 2247.

Correspondence.

"TOFRANIL."

SIR: I was interested to read the account of the impressions gained by Dr. Alan Stoller and his field-workers of the value of "Tofranil" (MED. J. AUST., March 12, 1960). My own experience with this drug approximates in general that set out in the article, although, as a non-Freudian, I would prefer to describe one of the signs of improvement as a renewed interest in the world outside rather than as "a re-investment of energy from internalized super-ego to the world outside". In fact, I am not quite sure what this statement means.

There is one suggestion in the article that I would question, and that is that parenteral administration seems to offer no special advantages. My own impression has been that, while with oral therapy alone the severe cases of depression (requiring hospitalization) seldom show much response under two weeks, intramuscular therapy often produces improvement in four to five days. In fact, if such therapy does not produce signs of improvement within the first week, I begin to query whether "Tofranil" alone will be effective and tend to supplement it with electro-convulsant-treatment. With hospital costs at their present level, this "prognostic" use of intramucular therapy seems to me not unimportant. A further indication to me of the added potency of intramuscular "Tofranil" is the slump that sometimes occurs when one tries to switch over entirely to oral administration on about the twelfth day. A reversion to approximately 50 mg. daily of "Tofranil" intramuscularly for some days, in addition to the usual oral dosage, has generally corected this tendency.

"Tofranil" is undoubtedly a promising drug, and the reactions of different groups of patients to varying combinations of the drug are worthy of careful observation. I was glad to note, however, Dr. Stoller's warning against premature claims that it might supplant electro-convulsant therapy. Such claims were blazoned forth a few years back for the reserpine-"Largactil" combination, but electro-convulsant therapy seems to have withstood the challenge comfortably, as reserpine is hardly heard of in psychiatry today.

Yours, etc.,
F. G. PRENDERGAST.

254 St. George's Terrace,
Perth, W.A.
March 24, 1960.

GENERAL PHARMACEUTICAL BENEFITS.

SIR: We are firmly convinced that the new *Pharmaceutical Benefits Act* has been introduced not as a health measure, nor even as an economical one, but as a piece of blatant political manœuvring. It is certainly not in the best interests of patients—and let us not forget that we exist for our patients. The Government's propaganda claims that most prescriptions written by doctors will now be available under the scheme; prior to March, 43% of all scripts were N.H.S. and 7% on P.M.S., so that it would be truly amazing if the addition of even a few useful items had not made the total 51%. This is the Government that we helped to elect.

We consider that the time for moderate, reasoned, careful negotiation has been allowed to slip past. The Federal Council had no franchise to accept such a monstrous political intrigue, and we want to dissociate ourselves from its action. We would even suggest that a new Association be formed at once, at the local level, and that those who at present take it upon themselves to dicker vainly with ill-formed persons be laughed into a limbo of forgotten things.

Let us state further that the day when the profession was a profession is fast fading; hence, as a body, the Association should use every method of modern advertising

such as regular full-page newspaper advertisements, a weekly television programme and several spot radio announcements each day to tell people the truth about Pharmaceutical Benefits. After all, the Government can do it, and so can the family chemist.

Yours, etc.,
I. SEGAL,
B. PITTS.

Cnr. Bondi Road and Denham Street,
Bondi, N.S.W.
March 28, 1960.

SIR: My faith in the medical fraternity in Australia, which has been badly shaken by recent events, is gradually being restored by the letters which have appeared in the latest issues of THE MEDICAL JOURNAL OF AUSTRALIA.

There is some spirit left; but are we merely going to follow the sorry example of our colleagues in Britain, who said "No! No!" as they were led along by the nose? Or is the proposed formation of the Australian Medical Association prophetic of a resurgence of the spirit which has made Australia and Australians admired and respected throughout the world?

As a parting thought I quote the serenity prayer of Alcoholics Anonymous, not facetiously, but in all sincerity:

> God grant me the serenity to accept the things I cannot change, courage to change the things I can, and the wisdom to know the difference.

Simply a G.P.,

Yours, etc.,
BRUCE PATERSON.

Alma Street,
Wee Waa, N.S.W.
March 28, 1960.

SIR: No one could disagree with the logical statements of Dr. Stuckey.

Now that we have had time to study the scheme, a referendum of all members of the B.M.A. would convince politicians and our Federal Council of our sentiments.

Yours, etc.,
W. D. CUNNINGHAM.

141 Macquarie Street,
Sydney, N.S.W.
March 30, 1960.

THE PROBLEM OF INJURY AND ACCIDENT.

SIR: It is heartening to read letters in your Journal referring to the accident problem in this State.

Dr. Paul has stated a truism when he writes that : "The establishment of accident units should have first priority—(i) to save life; and (ii) to prevent or minimize disability." If ever a State or country was in need of an organized accident service, it is New South Wales. The death rate from motor-car accidents on present figures could reach 1000 for this State by the end of 1960, which must make it one of the most dangerous States in the world in which to drive a motor-car. But, he points out, the establishment of accident units is in the doldrums. That this is so is possibly because, to be efficient and achieve their purpose, a completely different organization to that which at present is found in our large hospitals, running at quite a different *tempo*, is required. Again, if the organization is to be effective, many accident centres sited at strategic points and centred on major hospitals are necessary. The authorities at Royal Prince Alfred Hospital must be congratulated for making a start in organizing a service to deal with this increasingly complex and expanding branch of surgery.

To the problem of the subdivision of surgical labours in the treatment of the seriously injured, to which Dr. Paul obliquely refers, reference is made in the excellent memoranda of the Orthopædic Association of 1943 and 1959; these memoranda, dealing with the staffing of accident services, tend to make a segmental structure out of the seriously injured person, implying that successful treatment entails having a team of appropriate specialists immediately on call for twenty-four hours each day—i.e., a general surgeon to deal with abdominal injuries, an orthopædic surgeon to deal with bone injuries, a neurosurgeon to deal with head injuries, etc. But trauma of the present decade is not segmental, and on the contrary, in practice this system creates delays and difficulties which it is the object of the service to exclude.

The staff of the Birmingham Accident Hospital, who, one imagines, has had some experience in this problem, insists that one surgeon must undertake complete responsibility of the patient and they have stated their views on staffing in their recent publication, "Modern Trends in Accident Surgery and Medicine" (1959). I quote:

> In our experience the early treatment of many injuries, particularly road accidents, involves much more than a knowledge of orthopædic or plastic surgery; resuscitation requires surgical judgement which cannot be delegated to anæsthetists or transfusion officers except as part of a team. The surgeon must develop a general knowledge of the effects of injury in all parts of the body and be able to assess priorities; patients with multiple injuries cannot be sorted early and handed over to an appropriate specialist. Initial treatment requires surgeons with a wide knowledge of many fields and special experiences in injuries. Each consultant surgeon must be experienced in the orthopædic care of fractures, the treatment of wounds and abdominal surgery and have a sound working knowledge of the traumatic aspects of cranial, thoracic and plastic surgery. It is irrelevant whether he is called a traumatic surgeon, a general surgeon with traumatic experience, or an orthopædic surgeon with wider interests. It is the man, his interests, training and experience and not the terminology that matters. This does not mean that there is no place for the specialist thoracic or plastic surgeon or neurosurgeon in traumatic work. On the contrary, they often play a vital part, their advice and skill must be available readily and fully used when required.

I doubt whether the choice of an anæsthetist for the post of administrative head would be generally approved; this man must have had a wide surgical experience and "know" trauma in all its aspects.

The establishment and working of accident units require a lot of new thinking on the part of everyone. A modification of the fracture services envisaged for 1939 is not a suitable basis for the expanded accident services required in 1960. It is to be hoped that the apparent indifference to the experiences of the surgeons of the Birmingham Accident Hospital will change.

Yours, etc.,
J. C. FITZHERBERT.

387 Crown Street,
Wollongong, N.S.W.
March 21, 1960.

THE MEETING OF THE FEDERAL COUNCIL.

SIR: The ever-expanding influence of politics on medical practice demands of us all a more active interest in our Federal Council and its decisions. That such interest is not lacking may be judged by the numerous letters in THE MEDICAL JOURNAL OF AUSTRALIA of March 26, which also reports the Council meeting held last month.

The portion of this report headed "Specialist Surgeons" must surely evoke considerable comment. I am not familiar with the definition of a specialist to which reference is made, but the proposal of the College of Surgeons to produce a register of specialist surgeons leads me to ask, why?

The decision to revoke this term in favour of "approved surgeon" goes some way towards providing an answer. Approved to do what, and by whom? I note further that the register is at present a "domestic" record, but it is later hoped to be placed on a national State level. Ultimately, of course, it could become a public register, whether this be intended or not. Would this be in the best interests of the public or our surgical colleagues? The next step no doubt would be a register of "approved" gynæcologists, proctologists, urologists, cardiologists, etc. That the Minister for Health for New South Wales appreciates this fact is evidenced by his stated reply.

No one will deny that the complexities of present-day medical practice demand an increasing number of specialists; no general practitioner would presume to cope with the lot. However, such a step as proposed brings him a little nearer the stage where he will need an F.R.C.S. to incise a boil. No register will ever guide our decisions and practices so accurately as will our consciences and ethics. Our M.B., B.S. confers on us all the licence to do what we feel qualified to do in any field. Not all of us perhaps abide by the decisions of conscience—other less worthy motives may be cited; but the "approving" of specialists in all fields will do little to alter these fortunately rare anomalies.

Would it not be better to preserve what unity we have, rather than to commence a painful dissection of our

profession, removing each new secular group until left with the dry bones of the G.P. stripped of all initiative and status? The decisions of many hospitals not to encumber their staff with G.P.s has already dealt the profession a severe blow, for this denies the keen man a golden opportunity to further his knowledge.

If the profession is to guide its own destiny, the first aim must be unity. The proposed move would do no more than hasten our decay. Let us present a solid front, free of attempts to gain factional eminence.

Yours, etc.,

W. D. Jackson.

Pyramid Hill,
Victoria.
March 30, 1960.

MEDICAL RESEARCH IN AUSTRALIA.

Sir: I am glad that Dr. D. O. Shiels[1] has challenged Sir Facfarlane Burnet's[2] plans for the coordination of research in Australia, and pointed out the plan's dangers to freedom of thought.

It is true that biology needs a Newton or an Einstein to discover the simple laws which must underlie all the phenomena of life and disease. He will need to be a philosopher like Virchow, with profound historical insight and a sure instinct for separating the true from the false. The advance will require a detailed study of symptoms, and therefore a close association between doctor and patient. It will put technical methods in their proper place, and it will discourage chemical tests of no value to the patient, which damage the doctor's self-confidence.

Probably the truth about cancer or rheumatism would have been discovered long ago if we had not been hidebound by unproven theories (for example, that gout differs fundamentally from rheumatism, that metastases arise through transport of malignant cells), or confused by valueless statistics or blinded with brilliant techniques.

Great advances are being made in virology, Sir Macfarlane Burnet's own true field. More and more cytotoxic agents are being discovered; more and more diseases once vaguely called allergic or metabolic are found to be infections. In Australia notable discoveries have been made by F. J. Fenner[3] (eruptions in exanthems are not due to hypersensitivity, but to virus multiplying in the skin) and S. G. Anderson[4] (polyarthritis has been caused by a virus). It should now be accepted that viruses are probably the causative agents of many diseases (including cancer) which spread in the body or the skin. But "viruses should be considered as viruses because viruses are viruses".[5] Anyone who thinks that they are molecules or genes, or who tries to identify their chemical structure, is liable to get lost in a world of speculation.

A great deal of hypothesizing about genetics will cease when the lesson of "hereditary" mammary carcinoma in mice is learned. The infective agent is swallowed by the infant in its mother's milk,[6] and chromosomes and genes and mutations do not have to be involved. Another lesson which is slowly being absorbed is that many bacteria have L forms which are indistinguishable from viruses;[7] these probably enter the cells and account for the "allergic" sequelæ of infections.

Sir Macfarlane Burnet's approach through genetic chemistry has led him to a pessimistic conclusion which would mean the end of all research: "It is time that we stopped fostering the naïve expectations of the public that genetic anomalies, including feeblemindedness, cancer, the degenerative disabilities of age . . . will eventually be overcome as surely as we can deal with pneumococcal pneumonia or malaria."[8] I prefer to believe that we are on the threshold of a great advance in knowledge. Each important discovery has been a complete surprise to those who were the most familiar with the problem. In most cases, too, the new discovery has automatically suggested a previously unthought of means of treatment or prevention.

Yours, etc.,

Michael Kelly.

410 Albert Street,
East Melbourne.
April 1, 1960.

[1] Med. J. Aust., 1960, 1: 356 (February 27).
[2] Med. J. Aust., 1960, 1: 149 (January 23).
[3] *Lancet*, 1948, 2: 915 (December 11).
[4] Med. J. Aust., 1960, 1: 156 (January 30).
[5] Lwoff, A., 1957, *J. gen. Microbiol.*, 17: 239 (November)
[6] Bittner, J. J., 1958, *Ann. N.Y. Acad. Sci.*, 71: 943 (September 30).
[7] Edward, D. G., 1954, *J. gen. Microbiol.*, 10: 27 (January).
[8] *Brit. med. J.*, 1959, 2: 725 (October 17).

Medical Matters in Parliament.

HOUSE OF REPRESENTATIVES.

The following extracts from *Hansard* relate to the proceedings of the House of Representatives.

March 15, 1960.

Pharmaceutical Benefits.

Mr. McColm: I ask the Minister for Health: Is it a fact that, prior to 1st March, in some cases people who were to receive injections from their doctors would receive the injections when they first consulted the doctor in his surgery but that, subsequent to 1st March, it has become necessary for the patient to visit the doctor, obtain a prescription from him, take it to the chemist and get the material for the injection, then return to the doctor to have the injection? This entails two visits to the doctor instead of one, as well as in some cases the payment of 5s. towards the cost of the substance injected.

Dr. Donald Cameron: The position is, and always has been, that at some point in time the material for the injection has to be purchased from the chemist and conveyed to the doctor's surgery. The mechanism has not been altered by the new arrangements which have been made.

March 16, 1960.

Dental Services.

Mr. Luchetti: I ask the Minister for Health whether he has discussed with the Australian Dental Association the introduction of a dental scheme as a part of a national health plan. If such discussions have taken place, will he give special attention to the need for dental care of the children of Australia? Further, if the matter is receiving consideration, will the Minister say what stage this consideration has reached? When will he be in a position to announce his conclusions to the House?

Dr. Donald Cameron: This question has been considered from time to time but, so far, no really worth-while proposals have been put forward which would enable the introduction of a scheme of dental benefits.

Post-Graduate Work.

THE MELBOURNE MEDICAL POST-GRADUATE COMMITTEE.

Programme for May, 1960.

The Melbourne Medical Post-Graduate Committee announces the following programme for May, 1960.

General Practitioners' Refresher Course.

General Medicine and Surgery.

A course in general medicine and surgery will be held from May 16 to 20, at the Alfred Hospital. The programme is as follows:

Monday: 10 a.m., "Congenital Heart Disease", Dr. J. M. Gardiner; 11.15 a.m., "Ano-Rectal Conditions in General Practice", Mr. G. L. Grove; 12 noon, "Management of the Ischæmic Limb", Mr. I. L. McVey; 2.15 p.m., "Peptic Ulcer and its Management", Dr. P. J. Parsons; 3 p.m., "Carcinoma of the Breast and Therapy", Mr. James Guest.

Tuesday: 10 a.m., "Diagnosis of Common Gastro-Intestinal Conditions", Dr. J. E. Sewell; 11.15 a.m., "Acute Retention and Other Urological Problems in General Practice", Mr. K. Burnside; 12 noon, "Varicose Veins and Ulceration", Mr. N. T. Hamilton; 2.15 p.m., "Acute Cardiac Emergencies", Dr. M. C. Davis; 3 p.m., panel discussion, "Common Drugs and Their Use", chairman, Dr. Andrew; panel, Dr. Clarke, Dr. Kay and Dr. Doyle.

Wednesday: 10 a.m., "Diabetes and its Management", Dr. Ewen Downie; 11.15 a.m., "Psychosomatic Medicine in General Practice", Dr. W. R. Kingston.

Thursday: 10 a.m., "Chemotherapy", Miss J. Tolhurst; 11.15 a.m., "Hypertension", Dr. A. J. Barnett; 12 noon, Red Cross Blood Transfusion Service Unit, Dr. J. Morris; 2.15 p.m., "Common Respiratory Infections", Dr. M. N. Allen; 3 p.m., "Coronary Disease", Dr. J. M. Gardiner.

Friday: 10 a.m., "Congestive Cardiac Failure—Its Recognition and Management", Dr. H. B. Kay; 11.15 a.m., "Common Skin Conditions", Dr. J. Summons; 12 noon, orthopædics, Mr. J. C. McNeur s Unit; 2.15 p.m., "Cerebro-Vascular Accident—Its Management", Dr. J. A. Game; 3 p.m., surgical panel discussion; chairman, Mr. Guest; panel, Mr. Rowlands, Mr. Lawson, Mr. Grove and Mr. Ogilvy.

The fee for the course is nine guineas, and enrolments should be made by May 2 with the Post-Graduate Committee at the address given below.

Demonstrations at the Victorian Eye and Ear Hospital.

Demonstrations at the Eye and Ear Hospital will be conducted by the honorary medical staff on Saturday, May 21, as follows:

Eye Section: 9.30 a.m., cases of interest to general practitioners, Dr. Geoffrey Sutherland; 11.15 a.m., illustrations (by transparencies) of common eye complaints, followed by a quiz session, Dr. Kelvin Lidgett.

Ear, Nose and Throat Section: 9.30 a.m., cases of interest to general practitioners, Mr. C. N. L. Cantor, Mr. Walter Williams, Mr. D. F. O'Brien; 11.15 a.m., demonstration of operating microscope, Mr. D. F. O'Brien.

All members of the medical profession are invited to attend these demonstrations, without fee.

Country Courses.

Bendigo.—On May 6, at the Bendigo Base Hospital, at 8 p.m., Mr. C. Hembrow will discuss "Management of Backache". Dr. M. Clark, 98 Mitchell Street, Bendigo, is the local secretary for this course.

Sale.—On May 7, at the Gippsland Base Hospital in the Nurses' Lecture Theatre, the following course will be held: 2 p.m., "Modern Aspects of Pulmonary Tuberculosis', Dr. J. Eric Clarke; 3.30 p.m., "Nephritis", Dr. J. Frew; 4.30 p.m., "Neurological Diagnosis in General Practice", Dr. John Billings; 8 p.m., quiz session.

The local secretary for the course is Dr. G. Baldwin, 54 Cunninghame Street, Sale.

Ballarat.—On May 26, at Craig's Hotel, Ballarat, at 8 p.m., Mr. E. S. R. Hughes will discuss "Anal Conditions". The local secretary for the course is Dr. I. C. Goy, 22 Rippon Street, Ballarat.

Fees.—The fees for attendance at these courses are at the rate of 15s. per lecture, but those who have paid an annual subscription to the Committee are invited to attend without further charge.

Flinders Naval Depot.

On May 18, at Flinders Naval Depot, at 2.30 p.m., Dr. P. Wilson will speak on "Overdosage of Sedative Drugs". This lecture is being given by arrangement with the Royal Australian Navy.

COURSE IN MEDICINE, JUNE-JULY.

Entries close on May 23 for the course in medicine suitable for candidates sitting for the degree of M.D. (Melbourne) or M.R.A.C.P. They should be lodged with the Post-Graduate Committee.

ADDRESS.

The address of the Melbourne Medical Post-Graduate Committee is 394 Albert Street, East Melbourne. Telephone FB 2547.

THE POST-GRADUATE COMMITTEE IN MEDICINE IN THE UNIVERSITY OF SYDNEY.

Library Bulletin.

THE Post-Graduate Committee in Medicine in the University of Sydney announces that, by arrangement with the Postgraduate Medical School of London (University of London), from May 2, 1960, it will distribute weekly in Australia the Library Bulletin of the Postgraduate Medical School of London.

The Bulletin lists the contents and authors in some 358 journals currently received by the Postgraduate Medical School. The service will be subsidized by the Post-Graduate Medical Foundation of the University of Sydney to enable the charge to subscribers to be fixed at three guineas *per annum*.

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED MARCH 12, 1960.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.	Australian Capital Territory.	Australia.
Acute Rheumatism	2	..	2	..	..	..	..	..	4
Amœbiasis	..	..	..	..	..	..	..	..	..
Ancylostomiasis	..	..	..	..	..	..	10	..	10
Anthrax	..	..	..	..	..	..	..	..	..
Bilharziasis	..	..	..	..	..	..	..	..	..
Brucellosis	..	..	..	..	..	..	..	..	..
Cholera	..	..	..	..	..	..	..	..	..
Chorea (St. Vitus)	..	..	..	..	1	..	..	..	1
Dengue	..	..	..	..	..	..	..	..	..
Diarrhœa (Infantile)	5(4)	1(1)	4(4)	..	3(2)	..	5	..	18
Diphtheria	1	..	..	..	..	..	..	..	1
Dysentery (Bacillary)	..	..	..	2(2)	3(2)	..	3	..	8
Encephalitis	..	1(1)	..	..	..	..	..	..	1
Filariasis	..	..	..	..	..	..	..	..	..
Homologous Serum Jaundice	..	..	..	..	..	..	..	..	..
Hydatid	..	..	..	..	..	..	..	..	..
Infective Hepatitis	40(20)	17(11)	10(7)	17(12)	6(1)	..	..	..	90
Lead Poisoning	..	..	5	..	..	..	..	..	5
Leprosy	..	..	..	..	..	..	..	..	..
Leptospirosis	..	..	3	..	..	..	..	..	3
Malaria	..	..	5(5)	..	..	..	..	..	5
Meningococcal Infection	1	2(1)	..	..	..	..	..	..	3
Ophthalmia	..	..	..	..	9	..	..	..	9
Ornithosis	..	..	..	..	..	..	..	..	..
Paratyphoid	1(1)	..	..	..	..	..	..	..	1
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	..	..	..	..	..	..	..	..	..
Puerperal Fever	3(1)	..	..	..	..	..	..	..	3
Rubella	..	2(2)	..	3	..	..	..	..	5
Salmonella Infection	..	..	..	..	..	..	..	3	3
Scarlet Fever	12(4)	9(2)	..	1(1)	1(1)	..	..	..	23
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	..	..	2(1)	..	..	..	..	..	2
Trachoma	..	..	..	..	6	..	1	..	7
Trichinosis	..	..	..	..	..	..	..	..	..
Tuberculosis	30(15)	16(3)	37(9)	2(1)	..	1	..	..	86
Typhoid Fever	1(1)	..	2(1)	..	..	..	..	..	3
Typhus (Flea-, Mite- and Tick-borne)	..	..	2	..	..	..	..	..	2
Typhus (Louse-borne)	..	..	..	..	..	..	..	..	..
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] Figures in parentheses are those for the metropolitan area.

The Post-Graduate Committee will supply upon request and free of charge a sample copy of the Bulletin and a list of the journals which are used. Inquiries and subscriptions should be addressed to the Honorary Director, The Post-Graduate Committee in Medicine, 131 Macquarie Street, Sydney.

Course for the Diploma in Dermatological Medicine.

The Post-Graduate Committee in Medicine in the University of Sydney announces that a part I course for the diploma in dermatological medicine will be held in Sydney from May 9, 1960, for a period of 12 weeks. All lectures and demonstrations are held in the afternoons only, the fee for attendance being 50 guineas.

Early enrolment should be made to the Course Secretary, The Post-Graduate Committee in Medicine, 131 Macquarie Street, Sydney, from whom further details may be obtained. *Telephones:* BU 4497-8. Telegraphic address: "Postgrad Sydney".

Notes and News.

Medical Needs of the Community.

Over the past few months an ad-hoc committee appointed by the Council of the Victorian Branch of the B.M.A. has been considering the problem of the training of doctors in Victoria in relation to the medical needs of the State. The deliberations of this committee have been completed and its recommendations, incorporated in a report, have been submitted to the Honourable the Premier. The Committee recommended the appointment by the Government of a Standing Committee on Tertiary Education and suggested the establishment of a Standing Advisory Committee within the profession—composed of representatives of the B.M.A., the Royal Colleges and other professional bodies—to inquire into ways and means of improving the present facilities.

International Symposium on the Liver.

The second International Symposium on the Liver will be held on June 29 and 30, 1960, at Chianciano-Terme (Siena), Italy, under the auspices of the journal *Il Fegato*. The secretaries are Professor C. Cervini and Dr. O. Michetti, and information may be obtained by writing to them at the following address: Via Nicolo Porpora, 9, Roma.

Medical Practice.

POLICE OFFENCES (AMENDMENT) ACT, 1908, OF N.S.W. AS AMENDED.

The following notice appeared in the *Government Gazette of the State of New South Wales*, No. 33, of March 4, 1960.

POLICE OFFENCES (AMENDMENT) ACT, 1908, AS AMENDED.

Withdrawal of Drug Authority.

It is hereby notified for general information that in pursuance of the provision of Regulation 25 of the Police Offences (Amendment) Act, 1908, as amended, the authority of Dr. William Hubbard Fee to procure and be in possession of drugs to which the said Act applies for the purpose of his profession and to issue prescriptions for such drugs, is withdrawn as on and from the 21st March, 1960. (A. 59-188).

C. A. KELLY,
Chief Secretary.

Nominations and Elections.

The following have applied for election as members of the New South Wales Branch of the British Medical Association:

Bokor, Peter Paul, M.D., 1954 (Univ. Budapest), 10 Palmerston Avenue, Bronte.

Mulvey, Peter Maxwell, M.B., B.S., 1957 (Univ. Sydney), 7 Lovejoy Street, Mudgee.

Tarlinton, Michael John Kevin, M.B., B.S., 1956 (Univ. Sydney), 111 Pittwater Road, Boronia Park.

Diary for the Month.

April 18.—Victorian Branch, B.M.A.: Finance Subcommittee.
April 19.—New South Wales Branch, B.M.A.: Medical Politics Committee.
April 20.—Western Australian Branch, B.M.A.: General Meeting.
April 20.—Victorian Branch, B.M.A.: Clinical Meeting—Bacteriology Department.
April 21.—New South Wales Branch, B.M.A.: Clinical Meeting.
April 21.—Victorian Branch, B.M.A.: Executive of Branch Council.
April 22.—New South Wales Branch, B.M.A.: Ethics Committee.
April 22.—Queensland Branch, B.M.A.: Council Meeting.
April 23.—Queensland Branch, B.M.A.: Fifth Branch Convocation.
April 26.—New South Wales Branch, B.M.A.: Hospitals Committee.
April 26.—Tasmanian Branch, B.M.A.: Southern Subdivision.
April 27.—Victorian Branch, B.M.A.: Branch Council.
April 28.—New South Wales Branch, B.M.A.: Branch Meeting.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney): *All contract practice appointments in* New South Wales.

South Australian Branch (Honorary Secretary, 80 Brougham Place, North Adelaide): *All contract practice appointments* in South Australia.

Editorial Notices.

ALL articles submitted for publication in this Journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations, other than those normally used by the Journal, and not to underline either words or phrases.

Authors of papers are asked to state for inclusion in the title their principal qualifications as well as their relevant appointment and/or the unit, hospital or department from which the paper comes.

References to articles and books should be carefully checked. In a reference to an article in a journal the following information should be given: surname of author, initials of author, year, full title of article, name of journal, volume, number of first page of article. In a reference to a book the following information should be given: surname of author, initials of author, year of publication, full title of book, publisher, place of publication, page number (where relevant). The abbreviations used for the titles of journals are those of the list known as "World Medical Periodicals" (published by the World Medical Association). If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors submitting illustrations are asked, if possible, to provide the originals (not photographic copies) of line drawings, graphs and diagrams, and prints from the original negatives of photomicrographs. Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary is stated.

All communications should be addressed to the Editor, THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, New South Wales. (*Telephones:* MW 2651-2-3.)

Members and subscribers are requested to notify the Manager, THE MEDICAL JOURNAL OF AUSTRALIA, Seamer Street, Glebe, New South Wales, without delay, of any irregularity in the delivery of this Journal. The management cannot accept any responsibility or recognize any claim arising out of non-receipt of journals unless such notification is received within one month.

SUBSCRIPTION RATES.—Medical students and others not receiving THE MEDICAL JOURNAL OF AUSTRALIA in virtue of membership of the Branches of the British Medical Association in Australia can become subscribers to the Journal by applying to the Manager or through the usual agents and booksellers. Subscriptions can commence at the beginning of any quarter and are renewable on December 31. The rate is £6 per annum within Australia and the British Commonwealth of Nations, and £7 10s. per annum within America and foreign countries, payable in advance.